THE AMERICAN JOURNAL OF Clinical Nutrition

MARCH–APRIL 1957 VOLUME 5, NUMBER 2

Symposium on

Nutrition and Behavior*

THE study of the relationship of behavior to nutrition falls in an interstitial area, with its counterparts in such fields of human biology as the study of human work and of aging (gerontology). Interdisciplinary in nature[1] it shares with these counterparts the intellectual appeal and the practical importance as well as certain difficulties inherent in this type of endeavor—such as attracting financial support and adequate personnel.[2]

The complex relationships between diet and behavior[3] may be considered with reference to their *direction* (sequence of events) and to the *levels* at which they may be expressed. Thus, the psychotic behavior of a pellagrin illustrates the somatopsychologic sequence initiated by faulty nutrition. By contrast, in anorexia nervosa the individual starves himself, perhaps to death, in the absence of organic interference with the ingestion and digestion of food and in the midst of a plentiful food supply. This is, typically, a psychosomatic disorder.

While such neat schemes may appeal to the logician, the reality is frequently more complex, with socio-economic and attitudinal factors being at the root of improper nutrition (in this example, deficiency in niacin and tryptophan). This, in turn, brings about alterations in blood chemical constituents, brain metabolism and function, and, finally results in observable abnormalities of behavior.

This brings us to the problem of *levels* at which we wish or are able to study the events. The selection of levels, on which attention is to be focused, will depend on several factors, such as, the aims of the study, technical facilities, and the current status of methodologic development. Let us begin by agreeing firmly, first of all, that there are several levels requiring radically different technics. Ideally, if understanding of the somatopsychologic process is our goal, one should like to trace the successive steps in detail, including an analysis of the diet, alterations in the internal environment of the organism, and physiologically characterized changes

* Held with the cooperation of the National Vitamin Foundation, Inc., New York on April 27, 1956 at the Laboratory of Physiological Hygiene, under the sponsorship of the School of Public Health, University of Minnesota.

in the function of the central nervous system, as well as the behavioral facts and histopathologic findings.

Problems of this complexity must be studied in an interdisciplinary setting as no single individual can put on the hat, in turn, of the dietitian, biochemist, physiologist, pathologist, and psychologist. In clinical research the "team" is enlarged by the inclusion of internists, neurologists, and psychiatrists. The skills of psychiatrists are essential where individual psychotherapy is a part of the study, e.g., in some cases of weight reduction. In this laboratory psychiatric competence and collaboration were also found useful in severe, experimentally induced nutritional stresses.[4,5] When we leave the premises of the laboratory and the medical clinic, and this on occasion we must do, we need the professional help of the social scientist, preferably one with an anthropologic bent. This may lead us into the study of economics and agriculture, an approach that appears to be basic to the improvement of the nutritional status in the underdeveloped and underfed parts of the world.

The canvas is vast, almost overwhelming. Yet, within this perspective there is place for research on partial problems and for improvement of methodology.[6,7] It is in this way that scientific progress is actually made. For science usually marches in small steps; it is the exception rather than the rule that the individual scientist puts on "seven-league boots."

I have stressed, perhaps to excess, the complex character of the interrelationship between nutrition and behavior and the essentially interdisciplinary character of this field of study. Two specific points should be added. First, the chain cannot be stronger than its separate links. This emphasizes again the importance of developing better research methods and more adequate conceptual systems within the single disciplines. In particular, the crucial area of quantitative personality assessment is in need of such a development.

Second, in any interdisciplinary work everyone is a bit (and at times a good deal) uncomfortable. It is the very fact of *limited* personal competence that is the *raison d'etre* of the team approach to some of the separate problems and certainly to the field as a whole. I am sure that at this Symposium there will be times when the nutritionists will feel lost in the refinements of behavioral methods, while the psychologists will wish they knew more about biochemistry. The fact remains that we deal with nutrition *and* behavior, and that solid progress can be made only by *pooling* information and methods of physiologic and behavioral sciences. This Symposium should serve to document, in a measure, the effectiveness and the desirability of such an approach.

No attempt will be made to cover the whole field. Little or nothing will be said about such relevant topics as nutrition with reference to industrial work,[8] vision,[9] children's feeding problems, undernutrition due to psychologic maladjustment, or the psychiatric aspects of dieting other than that aiming at weight reduction.[10] Nevertheless, it is hoped that the papers to follow will indicate something of the geography of this border area and its contribution to the wider science of human nutrition.

JOSEF BROŽEK, PH.D.
Lab. of Physiological Hygiene
University of Minnesota

REFERENCES

1. BROŽEK, J., and KEYS, A.: Interdisciplinary research in human biology with special reference to behavior studies. *Am. Scientist* 33: 103, 1945.
2. BROŽEK, J., and KEYS, A.: General aspects of interdisciplinary research in experimental human biology. *Science* 100: 507, 1944.
3. BROŽEK, J.: Nutrition and psyche, with special reference to experimental psychodietetics. AM. J. CLIN. NUTRITION 3: 101, 1955.
4. KEYS, A., BROŽEK, J., HENCHEL, A., MICKELSEN, O., and TAYLOR, H. L.: *The Biology of Human Starvation.* U. of Minn. Press, 1950.
5. SCHIELE, B. C., and BROŽEK, J.: "Experimental neurosis" resulting from semistarvation in man. *Psychosomatic Med.* 10: 31, 1948.
6. BROŽEK, J.: Nutrition and performance in animals. In *Methods for Evaluation of Nutritional Adequacy and Status.* National Research Council, Washington, D. C., 1954, p. 155.
7. BROŽEK, J.: Physical performance. In *Methods for Evaluation of Nutritional Adequacy and Status,* National Research Council, Washington, D. C., 1954, p. 204.
8. SHILS, M. E.: Food and nutrition relating to work and environmental stress. *Modern Nutrition in Health and Disease,* M. G. Wohl and R. S. Goodhart, eds., Lea and Febiger, Philadelphia, 1955, p. 947.
9. STERN, J. J.: Nutrition in ophthalmology. In *Modern Nutrition in Health and Disease,* M. Wohl and R. S. Goodhart, eds., Lea and Febiger, Philadelphia, 1955, p. 861.
10. SELLING, L. S., and FERRARO, MARY ANNA S.: *The Psychology of Diet and Nutrition,* W. W. Norton, New York, 1945.

Impact of Diet on Behavior

THANKS to the generosity of the National Vitamin Foundation, to the hospitality of the Minnesota School of Public Health, and to the imagination and energy of Dr. Josef Brožek we have ahead of us what promises to be a stimulating and productive day. I am sure that I speak for all present when I say that we are grateful for the opportunity they have provided us for an interdisciplinary discussion of the problems of nutrition and behavior. Speaking for the psychologists present, may I add that this symposium is a welcome indicator of the growing realization not only that psychologic research has something to contribute to the science of nutrition but also, and more important for us, that nutritional studies can help to clarify some of the fundamental problems of human behavior.

There is no psychologic function—cognitive, affective or volitional—that is not related to the nutrition of the organism. There is no field of psychologic research, from the sensory acuity of night-flyers to the intellectual and temperamental differences among races, in which the nutrition of the individual could not become relevant. Let me mention two problem areas in particular in which, it seems to me, the nutritionist and the psychologist can profitably collaborate, viz., (a) the motivation of behavior, and (b) capacity for performance.

In recent years psychology has become more and more motivation-oriented. We are concerned with the initiation, the regulation and the direction of behavior; we are interested in needs, goals, and the machinery of energy transformations. The current pre-occupation with motivation stems initially from Darwin, but more recently from Freud. Without necessarily deploring the Freudian interest in sex, anxiety, and aggression, one welcomes a counterbalancing interest in the motivation of food-directed behavior. It is possible, we are told, to survive in a state of celibacy, even if this may be uncomfortable at times; but no one has ever demonstrated that survival is possible without food. Food is a basic need—according to the survival criterion—more basic than sex. But food-directed behavior involves much more than an organismic need. It includes appetites, remote goals and esthetic enjoyments that extend over the whole range of human motivation. When we search for paradigms for the understanding of the dynamics of behavior we can find none better than in the behavior of organisms directed towards food. No investigators have done more to clarify these problems than have Curt Richter and P. T. Young. It is our good fortune that we have both men as participants in this symposium, also representatives of the Quartermaster Food and Container Institute, where so many of the basic problems of food-directed behavior are being investigated.

The motivational problems belong, however, in later sessions. This session has to do with the impact of diet on behavior. From time immemorial it has been known that poorly fed animals are poor workers, although man seems to have been reluctant to correlate his own efficiency

with his diet. In recent years, however, the popular interest in diet has grown to fantastic proportions. Everywhere women (and men too) are counting their calories, swallowing vitamin pills, watching their mineral intake and subscribing to exotic diets. The poor nutritionist can hardly open his mouth without making the headlines as the advocate of a new dietary religion. Few sciences have suffered more from popular acclaim. In spite of the popular appeal of their subject, however, a core of dedicated scientists are seriously trying to find out how human efficiency is related to diet. The practical challenge is obvious: how can we through dietary regulation and education improve the lot of man? Behind this practical matter, however, are a multitude of scientific questions. What are the effects on human behavior of restricted caloric intake? of protein deficiency? of deficiencies in specific vitamins and minerals? Can human capacities be improved through dietary control? What is the relation between diet and temperament, or between one's diet and one's philosophy of life? The challenges to scientific curiosity seem limitless.

For the solution of most biologic, and of many social problems we must turn first to animals. In the study of nutrition we have made some headway in the analysis of human evidence; but for the crucial experiments we are still dependent on animals. In this session on "the impact of nutrition on behavior" we shall draw from both sources.

ROBERT B. MACLEOD, PH.D.
Dept. of Psychology
Cornell University
Ithaca, N. Y.

Psychologic Effects of Thiamine Restriction and Deprivation in Normal Young Men

By JOSEF BROŽEK, PH.D.*
With the technical assistance of HAROLD GUETZKOW,† PH.D.

THE present report is concerned with selected aspects of an interdisciplinary study on the relation of thiamine intake to "fitness." The study represented a logical sequel to the earlier work of this Laboratory,[1–4] including restriction of the vitamins of the B-complex for 161 days followed by 23 days of acute deprivation and 10 days of supplementation with thiamine alone.[5–8] The provision of thiamine was followed by a rapid return of appetite and regression of other symptoms and functional abnormalities. This indicated that thiamine was the crucial component. Consequently, in the present investigation the dietary restriction and terminal deprivation was limited to thiamine alone, other dietary components being provided in adequate amounts.

From the Laboratory of Physiological Hygiene, School of Public Health, University of Minnesota, Minneapolis, Minn.

* Professor, School of Public Health, University of Minnesota, Minneapolis, Minn.

† Present address: Graduate School of Industrial Administration, Carnegie Institute of Technology, Pittsburgh, Pa.

The data were collected under the terms of a contract with the Office of Scientific Research and Development. Important financial assistance was also provided by the Nutrition Foundation, Inc., the U. S. Cane Sugar Refiners' Association, N. Y., the Corn Industries Research Foundation, N. Y., Swift and Co., Chicago, the National Confectioners' Association, Chicago, the National Dairy Council, Chicago, and the Graduate Medical Research Fund, University of Minnesota. Merck and Co., Inc., provided a generous supply of pure vitamins. Most of the food materials were supplied by the Subsistence Branch, Office of the Quartermaster General, U. S. Army. The present report was prepared in the framework of investigations jointly supported, in part, by the Quartermaster General and the Surgeon General of the Department of the Army under Contract No. DA44-109-qm-1526.

Presented at a Symposium on Nutrition and Behavior held at the Laboratory of Physiological Hygiene, University of Minnesota, April 27, 1956, with the cooperation of the National Vitamin Foundation, Inc., New York and under the sponsorship of the School of Public Health, University of Minnesota.

DESIGN OF THE EXPERIMENT

The effects of a prolonged restriction and of a brief but acute deprivation of thiamine were investigated in a group of ten young men, clinically normal at the start of the experiment.

During the *standardization* period, about one month in duration, all men were maintained on an identical adequate diet and training schedule. The subjects became thoroughly familiar with the routine of "guinea-pig" life and a wide variety of test procedures. In those areas, such as motor functions, in which practice affects the test scores concerted effort was made to reach stable plateaus. The data obtained at the end of the standardization period served as "control" values for the evaluation of the effects of partial *restriction* (referred to as R in the text).

In this period a standard diet was served, consisting of ten daily menus served in rotation. The average daily caloric intake was about 3300 cal with carbohydrates, protein and fat contributing 54, 11, and 35 per cent of the total, respectively. The thiamine content of the standard diet was determined at frequent intervals and was found to vary only within narrow limits. Averaging mean values of the ten diets yields 0.612 mg as the daily dietary thiamine intake. As indicated in Table I, men in the "L" (low) group received placebos while the "M" (medium) and "H" (high) groups were given supplements of synthetic thiamine bringing their total daily intakes up to 1.01

TABLE I

Design of the Experiment. Size of Groups and Thiamine Intake During 6 Months of Partial Restriction.

Group	N	Mean thiamine intake, *mg/day*
L ("Low")	4	0.61 (Basal diet plus placebos)
M ("Middle")	4	1.01 (Basal diet plus 0.4 mg supplement)
H ("High")	2	1.81 (Basal diet plus 1.2 mg supplement)

NOTE: During subsequent acute deprivation the thiamine intake of all subjects was near zero. During supplementation 5 mg of thiamine were given per day to each man.

and 1.81 mg, respectively. The National Research Council recommended allowance of thiamine (1945 revision) was 1.5 mg vitamin B_1 for moderately active men (3000 cal) of average weight, or 0.5 mg per 1000 cal. The 1953 revision of the recommended allowance specifies 1.6 mg vitamin B_1 per day for young, moderately active (3200 cal) young men or, again, 0.5 mg/1000 cal.

The dietary supplement for all the subjects throughout the whole experimental period (restriction, deprivation, supplementation) contained: 2 mg riboflavin; 10 mg nicotinamide; 2 mg pyridoxine; 1 capsule containing vitamins A (5000 I.U.), and D (170 I.U.); 50 mg ascorbic acid; 5 mg calcium pantothenate; 1.3 g autoclaved yeast; 1 g choline hydrochloride, and a salt mixture. In partial restriction the subjects walked daily for two half-hour periods on a motor-driven treadmill (3.5 m.p.h., 10% grade). Additional exercise was provided by walking out of doors over a prescribed course, thus bringing the total daily energy expenditure to about 3300 cal.

Partial restriction was followed by a period of *acute deprivation* (D) during which all men were maintained on a diet considered adequate in all respects except for thiamine. The thiamine intake was decreased to the extremely low value of only 0.050 mg per day (0.015 mg per 1,000 cal). The period of deprivation varied from 15 to 27 days, according to individual resistance to this dietary stress. A good deal of effort went into making the thiamine-free diet of maximum palatability.[9] Four daily menus were prepared and served in rotation.

Before the acute deprivation period the thiamine excretion in the low-thiamine (no-supplement) group was close to zero. In the middle group (0.4 mg vitamin B_1 supplement) the average daily excretion for the 163rd and 164th day of restriction was 25 μg per day, in the high group (1.2 mg supplement) 188 μg per day. On the withdrawal of the supplements and of practically all the dietary thiamine, the thiamine excretion decreased to the average of 8 μg within 24 hours in the middle group and to near-zero in 48 hours. In the high thiamine group the average values of the two men decreased from 43 to 10 μg during the first four days of thiamine deficiency and zero or near-zero for the rest of the experimental period.

The scheduled physical work involved walking for two hours on the treadmill. As was true during the preceding months, there were occasional brief periods of anaerobic work associated with measurements of maximum oxygen intake or the Harvard Fitness Test involving running on the treadmill (8.5 per cent grade, 7 m.p.h.) until exhaustion or a maximum of five minutes.

In the period of *supplementation* (S) the same diet was continued but the men were given oral supplements of 5 mg thiamine per day.

METHODS

The methods used in this study followed the general pattern developed in previous work.[10] Observations will be reported on measurements of sensory functions, motor and intellective performance, and personality. The psychologic observations were carried out along with the study of biochemical and physiologic aspects of fitness. Parenthetically, it may be added that it is our general experience that performance in tests of sensory and intellective functions is surprisingly resistant to deterioration in nutritional stresses.

Items making up the self-ratings questionnaire are:

(1) Ability to concentrate
(2) Headache

(3) Patience with group members
(4) Ability to sleep at night
(5) Sense of humor
(6) General muscular weakness
(7) Mental alertness
(8) Ambition
(9) Apprehension
(10) Fatigability
(11) Interest in the project
(12) Nervousness
(13) Feeling of well-being
(14) Backache
(15) Numbness
(16) Irritability with project work
(17) Loss of appetite
(18) Burning sensations
(19) Forgetfulness
(20) Dizziness
(21) Muscle or joint pains
(22) Nausea
(23) Irritated by staff members

During the period of acute thiamine deprivation the questionnaires were filled out every four days and the ratings were based on the situation present during the preceding four-day period. The items were rated on a scale extending from 0 (normal, symptom absent) to +3 (very much more) and −3 (very much less than usual). In computing the scores as weighted sums of the items, all ratings indicating changes in the direction of deterioration were given a negative sign.

The Minnesota Multiphasic Personality Inventory (MMPI)[11,12] was developed in the framework of psychiatric diagnosis but it has also proven useful in experimental nutritional studies.[13,14] It may be scored with reference to a large number of scales, with transformed scores having a "normal" mean value of 50 and a standard deviation equal to 10. The scales constituting the "psychoneurotic triad"—hypochondriasis, depression and hysteria—have been shown to be particularly sensitive to experimentally induced nutritional deficiencies.

Cattell's Cursive Miniature Situations (CMS) personality test[15] consists of a moving strip, visible through a narrow opening and containing a variety of tasks. The speed of movement was 52.5 sec per strip. Eight strips were combined into a single unit, 176 in. long. The performance was evaluated in terms of a general score and two of the specific scores. The general score represents the number of correct responses (using the "wholistic" scoring, the maximum possible score was 136). The "emotionality" score is obtained as the number of errors (slanting lines crossed; the maximum was 269). The second specific measure, the "timidity" score, represents the ratio of points made in comparable tasks before and after the insertion of a surprise situation; a score above 1.00 indicates that the performance just after the "surprise" was poorer.

Intelligence was measured both by tests which took several hours to complete as well as by a battery of brief tests repeated at intervals of four days throughout the period of acute deprivation.[16] The C.A.V.D. intelligence scale belongs in the first category.[17] It consists of four subtests (Completions, Arithmetic, Vocabulary, Directions). There are 17 forms of the test, graded according to the difficulty of the items. In the present study the upper five levels (M,N,O,P,Q) were used, yielding a maximum possible score of 200.

In the area of sensory functions, determinations of flicker fusion frequency were included as a measure of sensitivity of the retino-cortical system.[18] A beam of light directed onto an opal glass plate was interrupted by a perforated rotating disc (Ref. 10, p. 1094). The rate of flicker was increased at a slow, constant rate until fusion was reported. An ambiguous cube, i.e., a cube design with a reversible perspective, was used in the test of perceptual fluctuation (*ibid*). Blinks were permitted at the 15th, 30th, and 45th sec during a one-minute period of fixation. Score is the average number of involuntary fluctuations of perspective obtained in three one-minute fixation periods separated by half-minute rest periods.

Auditory acuity was determined with a Maico D-5 audiometer, for the right ear. The average of three ascending threshold determinations was computed and used as a score. The measurements were made with tones of different pitch. Only the values obtained for tones with frequencies of 128, 2048, and 8192 d.v./sec were analyzed in greater detail.

The vibratory sensitivity was determined at two sites (external malleolus and sole of the foot, on the spot immediately posterior to the ball) using the "bone conduction" unit of the audiometer. The frequency of 256 d.v./sec was used consistently except for one subject who was always tested at 128 d.v./sec. The contact point of the vibrator, 0.65 cm in diameter, was applied each time at approximately the same spot with a pressure of 700 ± 100 g. The values, obtained as the average of three determinations, were expressed in terms of the bone-conduction figures of the hearing-loss dial. The pressure-pain threshold was determined by applying pressure to the calf by means of a sphygmomanometer. The scores, in mm of Hg, are averages of three successive determinations.

Capacity for motor performance is an important facet of "fitness." It is generally more sensitive to nutritional stresses than are intellective performance and sensory functions,[19,20] and was examined in considerable detail (Ref. 10, p. 1095 ff.). Except for those psychomotor tests in which specific reference is made to the frequency of determinations carried out during each testing session, the individual scores were obtained as the averages of two successive determinations.

Motor coordination was tested by having the subjects trace a grooved pattern while walking on the treadmill. This represents a complex task involving the coordination of eyes, hands and feet. The path was traced at a constant speed (one path unit per one sec). Performance was evaluated in terms of two scores: (1) the total number of errors, i.e., contact between the stylus and the sides of the path, and (2) the total duration of the contacts.

In the test of manual steadiness the subject was seated and held a stylus (0.5 cm in diameter) in a small opening (1.7 cm in diameter) in a metal plate. The amount of involuntary hand movement was recorded in terms of the number of contacts between the stylus and the metal plate. At each trial three 30-second testing periods separated by one minute of rest were used and the number of contacts was averaged.

In measuring body sway the subject stood erect for two minutes, with feet together and parallel, and with the eyes closed. The score for the ataxiometer represents the amount of anteroposterior movement, in cm.

Eye movements in reading were recorded by means of an ophthalmograph.[21] Equivalent 50-word passages were used in different testing periods. The performance was analyzed in terms of two scores: (1) the number of regressive eye movements per 100 words (regression score) and (2) the number of words read per 1/100 minute (speed score).

In the ball-pipe test of motor speed and coordination the score indicates the number of times a steel ball (marble) was passed through a 1-foot conduit pipe in 60 sec. In the 2-plate tapping test of motor speed the number of taps by a stylus during a 10-sec period was recorded.

In another test measuring the speed of movements, gross body-reaction times to visual stimuli while walking were determined. The response to the three stimuli, appearing in an irregular order and at irregular intervals, involved bending down and depressing the right the left, and both telegraphic keys. The reaction times were recorded in 1/100 sec. A score was obtained as the average of 50 reactions. It should be noted that this test as well as pattern tracing, ball-pipe, and tapping tests were performed while the subject walked on a motor-driven treadmill. The toe-reaction time to a simple auditory stimulus was measured with the subject seated. Again, 50 determinations were made and averaged, with the times recorded in 1/100 sec.

"Static" strength was measured by handgrip and back-lift dynamometers. The score, in kg, at a given testing session was obtained as the average of the two highest of three successive determinations.

Only data obtained prior, during, and following the period of acute thiamine deprivation will be presented here. The subjects were maintained on the thiamine-free diet until general debilitation and personality disturbances approached a critical level.

RESULTS

In general, the appearance of subjective symptoms and objective signs of deficiency

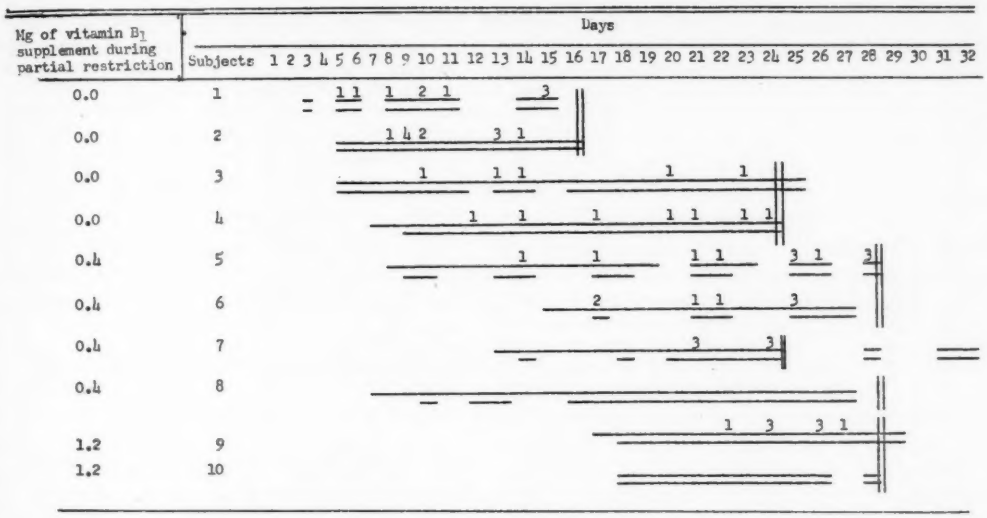

Fig. 1. Nausea and vomiting during acute thiamine deprivation and subsequent supplementation. Single horizontal lines indicate a slight nausea, double horizontal lines indicate a severe nausea (subject's ratings). The numbers above the lines refer to the frequency of vomiting on a particular day. The vertical lines indicate the start of thiamine supplementation (5 mg per day).

reflected the level of thiamine intake during the period of partial restriction. The men maintained previously on the highest intake were "protected" (i.e. did not develop symptoms of deficiency) longer (27 days) in comparison with those who were previously on the lowest thiamine intake (19 days). The men on the intermediary intake were also intermediary in reference to the onset of the symptoms but were closer to the high thiamine group (26 days). The course of the deficiency symptoms was much the same for all men.

The first signs of deficiency were anorexia and nausea. Vomiting first occurred in the previously lowest thiamine group on the 5th day, in the intermediary group on the 14th day, and in the high group on the 22nd day (Figure 1).

Results of neuropsychiatric examinations were summarized by Dr. B. C. Schiele on the basis of records available for nine subjects and are presented in Table II. Weakness, paresthesias, peripheral nerve involvement (including nerve trunk and muscle tenderness) and a change in mood were outstanding characteristics. Muscle weakness in one man (Number 4 in Table II) reached such a degree that he was unable to stand up from a squatting posi-

TABLE II

Neuropsychiatric Findings. Presence of a Symptom is Indicated by Letter X.

Subject Group Day of deprivation	1 L 10	2 L 13	3 L 22	4 L 22	5 M 23	6 M 26	7 M 26	8 M 25	9 H 25
Generalized weakness	X	X		X		X	X	X	X
Paresthesias		X	X	X	X		X		
Peripheral nerve involvement	X	X	X	XX	?			?	
Headache			X		X				
Feeling of being cold			X	X					
Marked irritability and depression	X	X	X	X	X				

TABLE III

Symptoms of "Neurasthenia" (Self-Ratings). The Score for Each Individual was Obtained as the Weighted Sum of 23 Items. Minus Sign Indicates Deterioration, Plus Sign Indicates Improvement. F = F. Tests of Statistical Significance of the Mean Changes During Deprivation (F_D) and Supplementation (F_S).

Group	R	D	S	Δ_D	F_D	Δ_S	F_S
L	−12	−28	+2	−16		+30	
M	− 8	−27	−8	−19		+19	
H	− 4	−10	−4	− 6		+ 6	
TOTAL	− 9	−24	−3	−15	10.8**	+21	17.6**

R = mean scores obtained at the end of *partial restriction*
D = mean scores at the end of maintenance on the thiamine-free diet (*deprivation*)
S = mean scores at the end of *supplementation*
Δ = mean change during deprivation (Δ_D) and supplementation (Δ_S)
F = test of statistical significance of the mean change during deprivation (F_D) and supplementation (F_S)
* = significance at the 5% level (reference value $F_{0.05} = 5.12$)
** = significance at the 1% level (reference value $F_{0.01} = 10.56$)

tion without help. This, plus other symptoms, including peripheral nerve involvement, indicated that we were dealing with an experimentally induced beri-beri. One man (Number 5), who showed a marked deterioration on some psychomotor tests involving timed responses, was characterized as "shaky and dizzy."

Self-ratings, referring to symptoms of "neurasthenia," showed a marked deterioration (Table III). Statistical tests indicate a highly significant negative change during thiamine deprivation and a remarkable recovery at the end of supplementation with this vitamin. This refers to the changes in the group as a whole (N = 10). However, the subscores of the men maintained on different supplement levels during the preceding period of partial restriction are of some interest, with the "low" group showing a larger change than the "high" group. The differences are even more striking when the recovery scores are considered as the reference point. Yet the uncertainties inherent in quantitative ratings of subjective symptoms cannot be disregarded, making inter-individual comparisons difficult.

TABLE IV

Mean Scores on Selected Scales of the Minnesota Multiphasic Personality Inventory. Increment = "Deterioration," Decrement = "Improvement." See Table III for explanation of symbols.

Group	R	D	S	Δ_D	F_D	Δ_S	F_S
Scale: "Hypochondriasis"							
L	52	84	50	32		−34	
M	48	75	49	27		−26	
H	48	62	43	14		−19	
TOTAL	50	76	48	26	38.9**	−28	38.7**
Scale: "Depression"							
L	73	93	54	20		−39	
M	57	73	62	16		−11	
H	70	75	62	5		−13	
TOTAL	66	82	59	16	6.9*	−23	14.9**
Scale: "Hysteria"							
L	68	85	63	17		−22	
M	64	79	65	15		−14	
H	62	66	56	4		−10	
TOTAL	65	79	62	14	13.7**	−17	26.5**

NOTE: On all these scales "normal" mean = 50, 1 standard deviation = 10.

The Minnesota Multiphasic Personality Inventory requires the respondent to answer in terms of "yes," "no," or "cannot say." The scores are based on a larger pool of items and their diagnostic significance was validated objectively. In acute thiamine deprivation there were large increments on the scales of the "psychoneurotic triad"—Hypochondriasis, Depression, and Hysteria (Table IV). The significance of the mean changes was examined in reference to the group as a whole (N = 10), with the result that both the increments (deterioration) in acute thiamine deficiency and the decrements (improvement) in the period of supplementation exceeded the 1 per cent level of statistical significance. The startling magnitude of some of these changes will be appreciated more keenly if the values of the "normal" mean (=50) and the standard deviation (=10) are kept in mind. There is a definite tendency for the men who had received no supplements in the period of partial restriction to show a greater degree of deterioration than the groups receiving supplements of 0.4 and 1.2 mg. of thiamine per day, respectively. The differences between the two supplemented groups suggest some advantage for the higher supplement but the differences are for the most part small and not completely consistent.

In contrast to the marked changes obtained on the MMPI, the performance in Cattell's Cursive Miniature Situations test (Table V) was essentially not altered. The general score showed a negligible decrement during thiamine deprivation, with the increment (recovery) during supplementation barely reaching the 5 per cent level of significance (the reference value $F_{0.05} = 5.12$). The "emotionality" score showed a small average increment at the end of deprivation, with a further increment at the end of supplementation. However, individual responses varied a good deal and the mean change in neither period was significant. Similarly, no significant increment was observed in "timidity."

Measured intellective functions remained surprisingly stable and free from deterioration, whether we used long tests (Thorndike's C.A.V.D.) or brief tests administered at four-day intervals, such as the battery measuring six "factors" (spatial perception, verbal fluency, perceptual speed, rote memory, number facility and inductive reasoning.) The only change reaching the 5 per cent level significance during supplementation was the improvement in the test of spatial perception which may be interpreted as reflecting a continuing practice trend.

There was a small decrement in flicker fusion frequency (Table VI) during deprivation followed by a larger and statistically highly significant increment during the recovery period. A slowing down was observed in the rate of perceptual fluctuations in the ambig-

TABLE V

Performance in Cattell's Cursive Miniature Situations Test of Character-Temperament for the Total Group (N = 10). For units see text (Methods). See Table III for explanation of symbols.

	R	D	S	Δ_D	F_D	Δ_S	F_S
General score	91	89	95	−2	0.38	+6	5.18*
"Emotionality"	23	27	30	+4	0.88	+3	0.82
"Timidity"	1.06	1.13	1.12	+0.07	0.38	−0.01	0.04

TABLE VI

Sensory Functions (N = 10)

	R	D	S	Δ_D	F_D	Δ_S	F_S
Flicker fusion frequency	43.6	43.0	44.4	−0.6	1.59	+1.4	9.45*
Perceptual fluctuation	23	19	23	−4	13.82**	+4	3.13
Vibratory sensitivity, malleolus	25	24	25	−1	0.39	+1	0.17
Vibratory sensitivity, sole	25	26	23	+1	1.17	−3	10.56**
Pressure pain threshold	180	153	168	−27	8.52*	+15	9.94*

TABLE VII
Motor Functions (N = 10)

	R	D	S	Δ_D	F_D	Δ_S	F_S
Eye-hand coordination, number of errors	39	44	31	+5	1.28	−13	21.12**
Eye-hand coordination, length of contacts	271	359	254	+88	4.70	−105	8.36*
Manual steadiness	15	20	13	+5	2.62	−7	8.59*
Body sway	21.0	25.4	19.3	+4.4	1.16	−6.1	1.65
Eye movements, regressions	16	14	13	−2	0.83	−1	0.25
Eye movements, speed score	3.1	3.3	3.6	+0.2	0.16	+0.3	1.97

TABLE VIII
Motor Functions (N = 10)

	R	D	S	Δ_D	F_D	Δ_S	F_S
Manual speed and coordination	75.6	68.6	77.0	−7.0	6.56*	+8.4	13.91**
Motor speed (tapping)	66.2	63.0	71.3	−3.2	4.30	+8.3	11.69**
Body reaction time †	46.3	51.1	48.2	+4.8	12.82**	−2.9	11.91**
Toe reaction time	28.1	31.3	28.7	+3.2	10.10*	−2.6	11.68**
Grip strength	58	56	55	−2	5.18*	−1	0.14
Lift strength	158	157	153	−1	0.15	−4	0.96

† N = 9 (omitting subject No. 5 with atypically long reaction times). Reference value of $F_{0.01}$ = 11.26.

uous-cube test, with a reversal of trend on supplementation. The mean size of the change was the same but the decrements during deprivation were more consistent.

Auditory acuity, at any of the three frequency levels of the stimulus that were examined in greater detail, and the vibratory sensitivity measured at the malleolus, were not affected. The vibration threshold determined at the sole of the foot showed negligible increment during deprivation. The change in recovery was somewhat larger and fairly consistent. It is not clear whether this should be considered as an indication of a real change, be it a small one, or a chance effect of random fluctuation. There is no doubt that the pressure-pain threshold decreased in thiamine deprivation. At the end of supplementation the recovery was not complete but it was statistically highly significant.

The means and F tests of significance of the changes in motor functions for the 10 men are given in Tables VII and VIII. The changes in eye-hand coordination during movement (pattern tracing) and in manual steadiness are in the direction of deterioration and there is a significant improvement on thiamine supplementation. Body sway increases during deprivation and is reduced during recovery but individual responses were highly variable. In one man, who may have suffered a spell of dizziness, a grossly atypical score (159 displacement units) was obtained. This value was not considered in calculating the group means in Table VII. With his score included the means for the three periods are 25.1, 38.8, and 21.6 units respectively. The F tests remain insignificant ($F_D = 1.88$, $F_S = 2.10$) because of the large interindividual variability.

Analysis of ophthalmographic records yielded no consistent changes, when either the number of regressive movements or the speed of reading was considered. The apparent trend toward a greater speed of reading, associated with a decrease in the number of regressions, is independent of the changing nutritional status.

There was a definite deterioration in the measurements involving speed of motion (Table VIII) whether one considers repetitive movements of the upper arm and hand (test of manual speed and coordination) or the tests of reaction time. In two-plate tapping the change in deprivation is also in the direction of deterioration but only the recovery during

supplementation is significant statistically.

In agreement with previous experience, but contrary to possible *a priori* expectations, there was minimal or no change in simple strength as measured by the hand-grip and the back-lift dynamometer. The decrement in grip strength during thiamine deprivation is negligible in terms of biologic importance and barely reaches the 5 per cent level of statistical significance.

The subgroups consisting of four men who received placebos during the period of partial restriction and six men who prior to acute thiamine deprivation had been given supplements (at the levels of 0.4 and 1.2 mg of thiamine per day) are too small for a detailed statistical analysis. Nevertheless, it may be noted that the changes in psychomotor functions tended to be larger in the "placebo" group. During thiamine deprivation in this group the increase in number and total duration of error contacts on the test of eye-hand coordination, decrements in the speed of tapping, and lengthening of the toe reaction time exceeded the 5 per cent level of the F test. In the "previously supplemented" the changes were for the most part in the same direction but did not approach statistical significance.

SUMMARY AND CONCLUSIONS

This study forms a link in a series of investigations of the impact of dietary variations on man's "fitness." The independent variables that were examined included vitamins, especially vitamins of the B-complex, calories[22] and—more recently—water.

The present study is concerned with the impact of a thiamine-free diet. It consisted of four periods: (1) a month devoted to standardization and collection of control measurements; (2) 168 days of partial restriction of thiamine, with respective daily intakes of 0.61 (N = 4), 1.01 (N = 4) or 1.81 mg (N = 2), and energy expenditure of about 3300 cal; (3) a period of acute thiamine deprivation, lasting 15 to 27 days during which all men received a thiamine-free diet and no thiamine supplements; and (4) a period of thiamine supplementation (5 mg per day for 9 to 21 days).

With other vitamins of the B-complex available in adequate amounts, the intake of 0.2 mg of thiamine per 1000 cal in our subjects, healthy young men, was at the borderline of deficiency.

In acute deprivation definite signs of deficiency developed in a matter of days or weeks. When the previously "thiamine-restricted," unsupplemented subjects were subsequently placed on a practically zero intake of thiamine, they exhibited a poor resistance to thiamine deficiency. This is an additional argument for considering the intake of about 0.2 mg of thiamine per 1000 cal as bordering on the inadequacy level.

Oral administration of thiamine was started for each man when it appeared that the deficiency had progressed as far as we considered safe. At this time general weakness and incoordination of the legs was very pronounced, anorexia was extreme, and hyperpyruvinemia was present. Thiamine supplements restored appetite and brought about a dramatic change in the attitudes of the subjects. The signs of peripheral neuropathy were more refractory. In one man definite residues, in the form of a peculiar gait, remained for several months.

Large changes in the direction of deterioration were observed during thiamine deprivation on the "psychoneurotic" scales of the Minnesota Multiphasic Personality Inventory; later these changes were reversed through thiamine supplements.

Within the limits of the experimental conditions, performance on tests of intelligence was not affected adversely by thiamine deprivation. There was a marginal decrement in flicker fusion frequency and the rate of perceptual fluctuations. In the sensory area the most consistent change, with statistically significant decrement in deprivation and return toward "normal" on supplementation, was observed in the pressure-pain threshold.

Manual speed and coordination, complex body reaction time and toe-reaction time exhibited a similar pattern of statistically significant changes. Motor speed (tapping), eye-hand co-ordination, manual steadiness, and body sway also exhibited deterioration in thiamine deprivation and recovery upon

supplementation but only one or the other change was statistically significant.

The nutritional status during the period of partial restriction was reflected in the tendency toward larger changes, in the direction of deterioration, among men receiving only the basal diet plus placebos prior to acute thiamine deprivation in comparison with the subjects who were given supplements (0.4 mg and 1.2 mg of thiamine, respectively). This differentiation was especially noticeable in the selected scales of the Minnesota Multiphasic Personality Inventory ("Hypochondriasis," "Depression," and "Hysteria"), and in several aspects of motor performance.

The significance of the present report is in its contribution to our information on the thiamine requirements of normal young men, and, in particular, in a comprehensive characterization of the psychologic changes associated with acute thiamine deficiency, reversed by means of nutritional supplementation. The effects of supplementation were dramatic both in the speed and degree of recovery.

REFERENCES

1. KEYS, A., and HENSCHEL, A.: Vitamin supplementation of U. S. Army rations in relation to fatigue and the ability to do muscular work. *J. Nutrition* 23: 259, 1942.
2. KEYS, A., HENSCHEL, A., MICKELSEN, O., and BROŽEK, J.: The performance of normal young men on controlled thiamine intakes. *J. Nutrition* 26: 399, 1943.

2a. KEYS, A., HENSCHEL, A., MICKELSEN, O., BROŽEK, J., AND CRAWFORD, H. H.: Physiological and biochemical functions in normal young men on a diet restricted in riboflavin. *J. Nutrition* 27: 165, 1944.

3. KEYS, A., HENSCHEL, A., TAYLOR, H. L., MICKELSEN, O., and BROŽEK, J.: Absence of rapid deterioration in men doing hard physical work on a restricted intake of vitamins of the B complex. *J. Nutrition* 27: 485, 1944.
4. HENSCHEL, A., TAYLOR, H. L., BROŽEK, J., MICKELSEN, O., and KEYS, A.: Vitamin C and ability to work in hot environments. *Am. J. Trop. Med.* 27: 259, 1944.
5. KEYS, A., HENSCHEL, A., TAYLOR, H. L., MICKELSEN, O., AND BROŽEK, J.: Experimental studies on men with restricted intake of the B vitamins. *Am. J. Physiol.* 144: 5, 1945.
6. BROŽEK, J., GUETZKOW, H., AND KEYS, A.: A study of personality of normal young men maintained on restricted intakes of vitamins of the B complex. *Psychosom. Med.* 8: 98, 1946.
7. GUETZKOW, H., AND BROŽEK, J.: Intellectual functions with restricted intakes of B-complex vitamins. *Am. J. Psychol.* 59: 358, 1946.
8. BROŽEK, J., GUETZKOW, H., MICKELSEN, O., AND KEYS, A.: Motor performance of normal young men maintained on restricted intakes of vitamin B complex. *J. Appl. Psychol.* 30: 359, 1946.
9. ANDERSON, MARIETTA, MICKELSEN, O., AND KEYS, A.: Diets and food items for the experimental production of thiamine deficiency in man. *J. Am. Diet. Assoc.* 22: 1, 1946.
10. KEYS, A., BROŽEK, J., HENSCHEL, A., MICKELSEN, O., AND TAYLOR, H. L.: *The Biology of Human Starvation.* University of Minnesota Press, Minneapolis, 1950.
11. HATHAWAY, S. R., AND MCKINLEY, J. C.: A multiphasic personality schedule (Minnesota). I. Construction of the schedule. *J. Psychol.* 10: 249, 1940.
12. WELCH, G. S., AND DAHLSTROM, W. G., *Basic Readings on the MMPI in Psychology and Medicine.* University of Minnesota Press, Minneapolis, 1956.
13. SCHIELE, B. C., AND BROŽEK, J.: "Experimental neurosis" resulting from semi-starvation in man. *Psychosom. Med.* 10: 31, 1948.
14. BROŽEK, J., AND ERICKSON, NANCY K.: Item analysis of the psychoneurotic scales on the MMPI in experimental starvation. *J. of Consulting Psychol.* 12: 403, 1948.
15. CATTELL, R. B.: An objective test of character—temperament. *J. Gen. Psychol.* 25: 59, 1941.
16. GUETZKOW, H., AND BROŽEK, J.: Intellective tests for longitudinal experiments on adults. *Am. J. Psychol.* 60: 350, 1947.
17. THORNDIKE, E. L., WOODGARD, ELLA, AND LORGE, I.: Four new forms of the I.E.R. Intelligence Scale for use on the college or higher levels. *School and Society* 42: 271, 1935.
18. SIMONSON, E., AND BROŽEK, J.: Flicker fusion frequency: Background and applications. *Physiol. Rev.* 32: 349, 1952.
19. BROŽEK, J., AND TAYLOR, H. L.: Tests of motor functions in investigations on fitness. *Am. J. of Psychol.* 67: 590, 1954.
20. BROŽEK, J.: Physical performance. In *Methods for Evaluation of Nutritional Adequacy and Status.* H. Spector, M. S. Peterson and T. E. Friedman, eds. National Research Council, Washington, D. C., 1954, pp. 204–211.
21. Bureau of Visual Science. *The Ophthalm-o-graph. The Metron-o-scope: Manual for Controlled Reading.* American Optical Co., Southbridge, Mass., 1937.
22. BROŽEK, J., AND TAYLOR, H. L.: Psychological effects of maintenance on survival rations (carbohydrate diet, 1010 calories per day, water *ad libitum*). *Am. J. Psychol.* 1957 (in press).

ADDENDUM: SOME BIOCHEMICAL DATA*

It may be useful to present some additional biochemical information concerning the diet and the metabolic state of the subjects. Data on the thiamine content of the individual diets and their variability, as determined by chemical analysis,[1] indicate that the mean of the 10 diet means is 0.612 mg, with average $\sigma_{\text{within diets}} = 0.105$ mg and $\sigma_{\text{between diets}} = 0.070$ mg All subjects were maintained during the first six months on this dietary regimen and received capsules containing 0, 0.4, or 1.2 mg of thiamine per day, respectively.

The average urinary excretions of thiamine and pyramin, the pyrimidine end-product of thiamine metabolism normally present in human urine,[2] are indicated in Table I. While thiamine excretion may be considered as an amount of vitamin wasted by the body, pyramin excretion presumably is more directly related to the metabolic utilization of this vitamin in the body. At daily thiamine intakes above 0.7 mg. per day, the thiamine excretion is linearly related to intake. Below 0.7 mg per day, the values are very close to zero. The small amounts reported in the urine may be due, in part to extraneous fluorescent materials in the urine. Thus, thiamine excretion data are of little value at these low intake levels. Pyramin excretion data, on the other hand, are of special importance under conditions of low thiamine intake. They approach a nearly constant excretion level at thiamine intakes above 2 mg per day.

TABLE I

Thiamine and Pyramin Excretion, mcg/24 hrs, in the Three Groups Maintained on Different Levels of Thiamine Intake*

Group	No. of subjects	Thiamine intake, mg	Thiamine excretion mean	Thiamine excretion σ within days	Pyramin excretion mean	Pyramin excretion σ within days
Low (L)	4	0.61	4.6	6.3	125.5	21.0
Medium (M)	4	1.01	26.2	15.9	171.5	22.9
High (H)	2	1.81	195.4	35.8	267.4	27.7

* The excretion levels refer to values obtained after a stabilization in excretion was reached following the change from a thiamine intake common to all subjects during the control period.

In trying to assess the metabolic state of the three groups of men at any particular time, a critical question arises as to how close they have come into equilibrium with their respective levels of thiamine intake. It is known that: (a) body reserves of thiamine are not large, and (b) severe deficiency signs occur within a few days when men are placed on a zero intake of this vitamin. These facts have been taken as evidence of a rapid metabolic adjustment to alterations in the intake. When thiamine intake is changed in the intake range between 1.0 and 2.0 mg per day, the thiamine and pyramin excretion levels adjust in such a way that in each successive ten-day period the mean excretion level changes by half of the remaining distance toward the new equilibrium level.[2] From this, one would expect approximately 90 per cent equilibration to be attained within a month on the new intake. One to two months should provide substantially complete equilibration. In the present experiment, it may be recalled the subjects were maintained on constant levels of 0.6, 1.0 and 1.8 mg/day for some six months before being placed on a zero-thiamine diet.

The problem of adaptation to this new level is of special interest in reference to the rate at which deficiency symptoms developed in the three groups (L, M, and H) when all men were placed on a zero intake of thiamine. Did increased levels of thiamine intake during the preceding six-month period provide a substantial degree of protection against the effects of the acute deficiency stress? The answer, in general, seems to be that there were no appreciable differences between the responses of the M (1.0 mg/day) and H(1.8 mg/day) groups.

* This material was obtained in cooperation with Dr. Olaf Mickelsen and Mr. Howard Condiff in the Laboratory of Physiological Hygiene, University of Minnesota.

The L(0.6 mg/day) group, on the other hand, deteriorated much more rapidly than either of these higher intake groups. This can be seen, for example, in the blood pyruvate data (Table II). There were no significant differences between the 1.0 and 1.8 mg/day groups either in the six-month restriction period or in acute deficiency. The blood pyruvate level of the 0.6 mg group, on the other hand, was somewhat elevated even during the restriction period, and it rose sharply in acute deficiency. On the tenth day of thiamine deprivation, pyruvate levels of the M and H groups were not far from those characteristic of the L(0.6 mg/day) group prior to the acute deficiency stress.

TABLE II

Average Plasma Pyruvate Levels, in mg per 100 ml Measured One Hour After Oral Administration of 100 g of Glucose

Group	Partial restriction		Acute deficiency	
	Thiamine intake, mg/day	Pyruvate in 6th mo	Thiamine intake, mg/day	Pyruvate on 10th day
L	0.61	1.3	0.05	2.0
M	1.01	0.9	0.05	1.5
H	1.81	0.9	0.05	1.3

There is a good correspondence between the picture emerging from these data and the changes in motor functions, personality, and general condition of the subjects.

All of these data seem to lead to two conclusions: (1) The intake of 0.6 mg of thiamine per day seems to be a suboptimal level for this group of men as shown by (a) their rapid deterioration when placed on a zero thiamine intake, (b) their elevated blood pyruvate levels, and (c) their substantially zero thiamine excretion levels. (2) Raising the level of thiamine intake above 1.0 mg/day provided, at best, only a few days of added protection.

W. O. CASTER, PH.D.
Dept of Physiological Chemistry
University of Minnesota

REFERENCES

1. MICKELSEN, O., CONDIFF, H., and KEYS, A.: The determination of thiamine in urine by means of the thiochrome technique. *J. Biol. Chem.* 160: 361, 1945.
2. MICKELSEN, O., CASTER, W. O., and KEYS, A.: A statistical evaluation of the thiamine and pyramin excretions of normal young men on controlled intakes of thiamine. *J. Biol. Chem.* 108: 415, 1947.

Effect of B-Complex Vitamins on Conditional Reflexes in Dogs

By W. Horsley Gantt, M.D.*

The stimulus for my interest in the effect of vitamin deficiencies on behavior came from the work of Dr. Max Wintrobe about 1940. After witholding for several months some of the vitamin B-complex from pigs, he noted the development of ataxia and other neurologic symptoms as well as changes in the motor cells of the spinal cord.[1–4] But the methods of examination did not permit an adequate evaluation of behavioral changes.

The reverse effect—of stress on eating habits—had already been observed in my studies of neurotic dogs. Thus, in one such dog I had seen negativism, hyperacidity, and refusal of food in a stress situation.[5] Other dogs became depressed from emotional shocks and did not eat for four or five days, and one young dog taken away from its home practically starved itself in the laboratory, ate again when returned home, and finally died in the laboratory from grief and starvation. We have a dog ("V3"), born in the laboratory, who in a period of over five years (since 1950) has never accepted food when any person is standing nearby. This includes the *Diener* who has always fed the dog and has never been involved in the experimentation. Dog V3 developed a "catatonic" condition several years ago with *cerea flexibilitas*, immobility, and sexual impotency except under alcohol.[6]

From the Pavlovian Laboratory, Johns Hopkins University, Baltimore.

* Associate Professor of Psychiatry, Johns Hopkins University; Director, Pavlovian Laboratory of the Phipps Psychiatric Clinic.

Presented at a Symposium on Nutrition and Behavior held at the Laboratory of Physiological Hygiene, University of Minnesota, April 27, 1956, with the cooperation of the National Vitamin Foundation, Inc., New York and under the sponsorship of the School of Public Health, University of Minnesota.

Concluding from the neuro-anatomic changes in Wintrobe's pigs that these neurologic changes would most likely be accompanied by impairment of the higher nervous activity measurable by the conditional reflex function, we undertook a study with Dr. Wintrobe on dogs.

METHODS AND OBSERVATIONS

Four dogs were subjected to a diet deficient in pantothenic acid or pyridoxine. These animals had been in the laboratory for several years during which time they elaborated conditional reflexes to different auditory stimuli connected with faradic shock to the foreleg (Fig. 1). When the animals had maintained a 100 per cent differentiation between two tones for some months they were given the deficient diet, which was quantitatively and qualitatively exactly the same as the control diet except that the vitamins, which had been given in capsules, were now omitted. After 4 to 15 days the animals showed disturbances in the conditional reflexes which became progressively worse; this disturbance consisted in failure to differentiate, notwithstanding repeated practice (Figs. 2 and 3). There were no observable behavioral or demonstrable neurologic changes (hopping, placing, tendon, or sexual reflexes). Return to the adequate diet restored the differentiation.

After several months of perfect differentiation the dogs were again put on the same deficient diet and there was again an impairment of conditional reflex equilibrium which was restored to normal a second time when the animals were returned to the adequate diet. Noteworthy was the loss of equilibrium between the conditional reflexes without any other observable changes in behavior of blood.

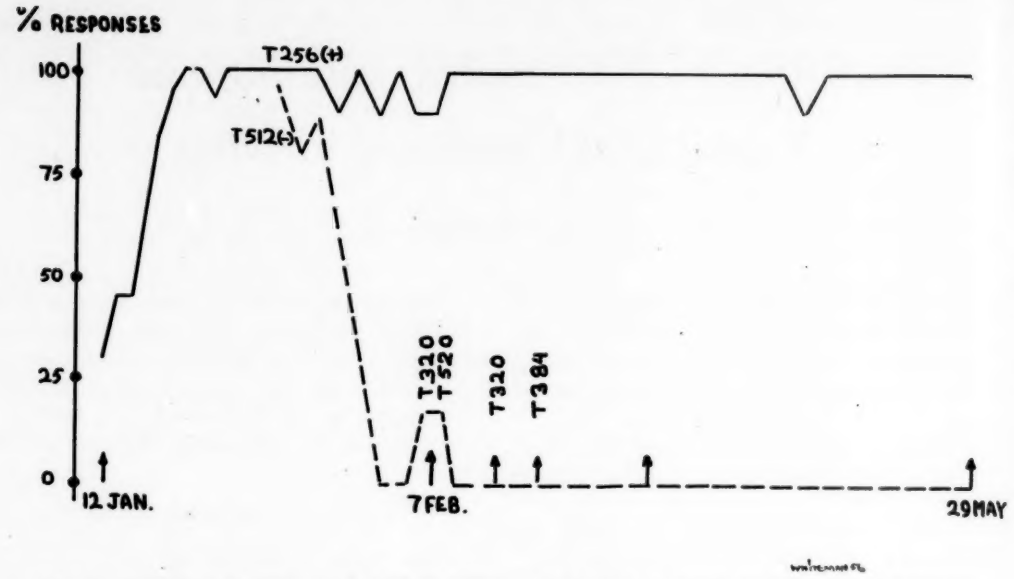

Fig. 1. Formation of excitatory conditional responses to T256+ (followed by shock) and inhibitory conditional responses to T512−, T320−, T520− and T384− (not followed by shock). Solid line shows the excitatory and the dotted line the inhibitory conditional responses. Perfect differentiation is 100 per cent for T256+ and 0 per cent for T512−.

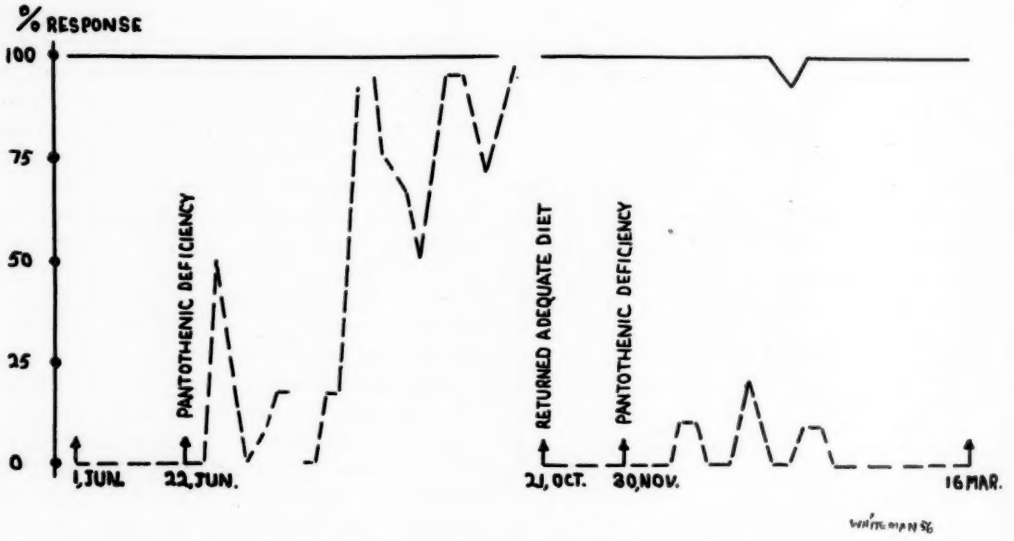

Fig. 2. Effect of pantothenic acid deficiency. Impairment of differentiation between T256+ (solid line) and T512− (dotted line) in four days after deficient diet. Perfect differentiation after return to an adequate diet. Subsequent deficient diet, November 30, causes less impairment.

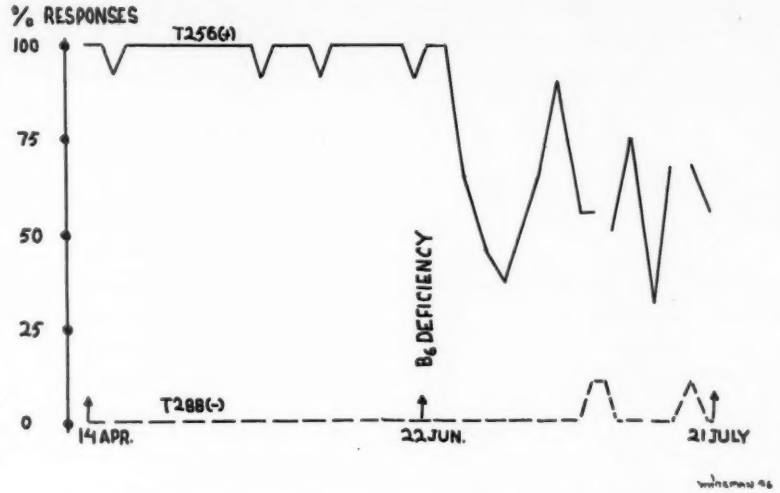

Fig. 3. Effect of pyridoxine deficiency. Note marked impairment differentiation within a few days after deficient diet, becoming worse during the next month.

DISCUSSION

Comparing the effect of this vitamin deficiency with other procedures we have used in the laboratory, the impairment in conditional reflex function is greater than that produced by 2 ml alcohol/kg although alcohol caused both marked neurologic changes including ataxia and personality modification. The effect is about the same as 3–5 mg/kg of morphine but morphine caused in addition a loss of equilibrium, drowsiness, and neurologic changes.[7] The loss of ability for differentiation is greater than that resulting from the exposure of the dog to an altitude of 18,000 feet for four hours and is equivalent to the effect of anoxemia caused by exposing the dogs to an altitude of 25,000 feet.[8] However, the impairment from anoxemia may last several months or may be irreversible, especially in old dogs, while the impairment from the vitamin deficiency is strictly temporary, being restored to normal within a few days after the return to an adequate diet.

Comparing the action of pantothenic acid deficiency with other agents, such as alcohol, morphine, mescaline, and anoxemia, this vitamin lack is almost entirely devoid of action on any measured function other than the conditional reflexes. This function, however, may be considered comparable to mental alertness and ability for learning. In hypothyroidism in humans we have shown that the conditional reflex function is markedly impaired, but that after thyroid extract administration it returns to normal parallel to blood cholesterol and basal metabolic rate.[9] Thus we may conclude that although a few days to a month of complete deprivation of pantothenic acid or pyridoxine may produce no neurologic or blood changes, this deficiency may seriously impair a mental function. This function is restored to normal, however, after a few days by the addition of the deficient vitamin to the diet.

REFERENCES

1. WINTROBE, M., MILLER, J. L., JR., and LISCO, H.: Relation of diet to occurrence of ataxia and degeneration in the nervous system of pigs. *Bull. Johns Hopkins Hosp.* 67: 377, 1940.
2. WINTROBE, M.: Thiamine deficiency in swine. *Bull. Johns Hopkins Hosp. 71*: 141, 1942.
3. WINTROBE, M.: Sensory neuron degeneration in pigs; protection afforded by calcium pantothenate and pyridoxine. *J. Nutrition* 24: 345, 1942.
4. WINTROBE, M.: Attempts to produce pernicious anemia experimentally. *New Eng. Med. Center* 3: 13, 1941.
5. GANTT, W.: *Experimental Basis for Neurotic Behavior*. Paul B. Hoeber, New York, 1944, p. 211.

6. GANTT, W.: Effect of alcohol on sexual reflexes of normal and neurotic male dogs. *Psychosom. Med.* 16: 174, 1952.
7. STEPHENS, J. H., and GANTT, W.: Effect of morphine on behavior. *Bull. Johns Hopkins Hosp.* 98: 245, 1956.
8. GANTT, W., THORN, G., and DORRANCE, C.: Anoxia on conditional reflexes in dogs. *Fed. Proc.* 8: 53, 1949.
9. GANTT, W., and FLEISCHMANN, W.: Effect of thyroid therapy on the conditional reflex function in hypothyroidism. *Am. J. Psychiat.* 104: 676, 1948.

Pantothenic Acid Deprivation and Thermal Behavior of the Rat

By BERNARD WEISS, PH.D.

PANTOTHENIC acid appears to be vitally implicated in the capacity to withstand stress, and its withdrawal provokes disturbances in a wide range of functions.[1] One of the ways in which a deficiency of this vitamin may be manifested is in structural deterioration and functional impairment of the adrenal glands,[1–6] a result due at least in part to the fact that most of the pantothenate in the tissues is bound as coenzyme A (CoA), essential to the synthesis of steroid hormones.[7] CoA is also essential to a great number of metabolic processes, such as fatty acid breakdown and carbohydrate metabolism, and its versatility as a biocatalyst has been amply demonstrated. Further evidence for its critical role in stress resistance comes from the finding that large doses of pantothenate appear to sustain tolerance to cold stress,[1] while deficiencies impair the ability to survive such stress.[1–8]

Another way in which the function of pantothenic acid may be studied is to observe its behavioral effects. Behavioral indices are useful because they provide a picture of the total organism at work, a condition which is sometimes necessary to reveal certain subtle changes produced by internal chemical states. One variant of such a condition is provided by a scheme in which the intensity of a stress may be diminished by an appropriate response on the part of the organism. In the present study, a situation was used in which the frequency of such a response provided an index of the impact of a cold stress.

From the Department of Experimental Psychology, School of Aviation Medicine, USAF, Randolph Air Force Base, Texas.

* Present address: Division of Clinical Pharmacology, Johns Hopkins Univ. School of Medicine, Baltimore 5, Md.

Presented at a Symposium on Nutrition and Behavior held at the Laboratory of Physiological Hygiene, University of Minnesota, April 27, 1956, with the cooperation of the National Vitamin Foundation, Inc., New York and under the sponsorship of the School of Public Health, University of Minnesota.

METHOD

Apparatus

A device commonly used by psychologists to measure the effects of different variables upon frequency of responding is the Skinner box.[9] As typically used, it consists of a cabinet which contains a lever or bar that can be pushed by an animal, and a means for the delivery of a "reward". In the most simple program, continuous reinforcement, a reward is given for each press of the lever.

The Skinner box provides, for certain purposes, an excellent means with which to gauge the physiologic state of an organism. For example, the rate of responding with food reinforcement is directly related to the length of time that the animal has been deprived of food (up to the point where the debilitation induced by prolonged starvation supervenes).

In this laboratory, the Skinner box has been modified* as shown in Figure 1, with the reinforcement for pressing a plastic lever provided by the activation of an infrared heat lamp while the animal is exposed to a low ambient temperature. Since this arrangement (unpublished data) leads to reliable differences in response rate as a function of temperature, it was expected that it would evoke different rates of responding from animals differentially affected by cold stress. The present data are based on an ambient box temperature of 0° C and a heat reward provided by a 250-watt infra-red

* By R. A. McCleary.

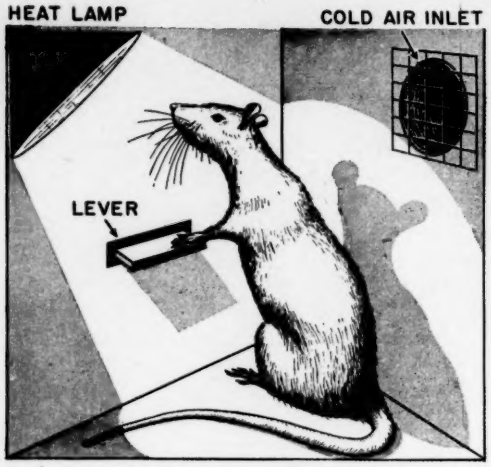

Fig. 1. Sketch of the modified Skinner Box using heat reinforcement.

heat reflector bulb which was activated for 10 sec by each lever pressing. The lamp extended to within 5.5 in. of the floor of the chamber, which measured 10 x 10 x 11 in.

Procedure

Sixteen male albino rats of the Sprague-Dawley strain, approximately seven months old, were used as subjects. After preliminary training in the Skinner box with food reinforcement and, later, heat reinforcement, half the animals were placed on a pantothenate-deficient diet and half on a pantothenate-supplemented diet and allowed to feed ad libitum.* Calcium pantothenate (Merck) was given to the supplemented group as a drinking solution in a concentration of 1 mg/10 cc. Each animal in this group was given 20 cc of the solution each night and received no other liquid the following day until it had been consumed. Drinking tubes with curved lips were used to prevent spilling of the solutions. This procedure insured that each animal in the group received 2 mg of calcium pantothenate daily.

Both groups of animals were then given practice in the Skinner box for four weeks, four hours per week. The coats were clipped at the beginning of the investigation and maintained in that condition throughout.

At the end of this time, no significant differences in response rate were evident. Indeed, no overt signs of pantothenate deficiency could be observed and weight gains and food consumption, as shown in Table I, were not significantly different, although a trend in the expected direction seems apparent. Moreover, all of the animals appeared to be less active than usual.

TABLE I

Mean Weight Gain from First to Fifth Week and Food Consumption for Fifth Week for Pantothenate-Deficient and Pantothenate-Supplemented Rats

		Weight gain g	Food consumption g
Supplemented	Mean	35.00	77.00
	S. D.	±17.29	± 9.80
Deficient	Mean	29.75	73.63
	S. D.	±22.21	±12.04

It was then hypothesized that the pantothenate deficiency was being compensated for, to some degree, by the unlimited intake of other nutrients. Beginning with week five, the animals were placed on a continuous reinforcement schedule for one hour daily. After six experimental days on such a schedule, a three-day starvation period was inaugurated. The day following this period, access to food was permitted for 30 minutes. An intervening day of starvation preceded another 30-minute feeding period and this schedule was continued to the end of the experiment. The investigation was ended when the group of pantothenate deprived animals had become so severely impaired physically that some died, making the reliability of further observations on the survivors questionable.

RESULTS

The results are summarized in Figure 2, which illustrates the conjoint effects on response rate of starvation and pantothenate deprivation. Prior to the starvation regimen the pantothenate-deficient group responded at only a slightly higher rate, but the diver-

* The basic diet was approximately the same as that used by Ershoff[8] and was supplied by General Biochemicals, Inc.

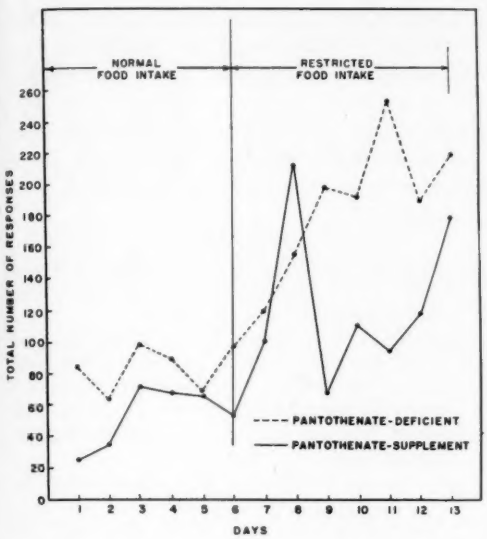

Fig. 2. Total number of responses per day for pantothenate-deficient and pantothenate-supplemented groups throughout the 13-day experimental period.

gence became greatly pronounced during food restriction. The greater frequency at day eight for the pantothenate-supplemented group was due to but two animals and is the only "impurity" in the trend. Table II gives

TABLE II

Mean Daily Response Rate and Variability Among Animals for Normal and Restricted Food Intake Periods and Differences Between Periods

		Normal	Restricted	Difference
Pantothenate-Supplemented	Mean	6.60	15.71	9.11
	S. D.	±6.00	±4.70	±4.02
Pantothenate-Deficient	Mean	10.44	23.61	13.20
	S. D.	±7.40	±10.77	±7.32

the mean and standard deviation for both periods and for the differences between periods.

Evaluation of the results by the analysis of variance and some supplemental procedures lead to the following statements:

(1) The starvation regimen produces a significant increase in response rate.

(2) The two groups differ significantly during the restricted period, the deprived group making significantly more responses.

(3) The deficient animals show somewhat greater variability.

DISCUSSION

These data demonstrate that what might be called the thermotactic drive can be intensified by at least two kinds of dietary restrictions. One is a reduction in total food intake. The other is a reduction in intake plus deprivation of pantothenic acid, the latter adding an extra increment of intensity.* It is analogous to the finding that hungry rats respond more frequently (with food reinforcement) than sated rats.

Another feature that deserves comment is the change in variability produced by the experimental treatment. Such a result is often obtained in experiments which expose groups of animals to different treatments. Its significance is not understood, but it appears so often in biologic research that it warrants more attention from experimenters, particularly because it indicates that the treatment has produced a significantly different population.

The fact that no effects related to pantothenate deprivation appeared until intake restriction was superimposed is an important aspect of the data. Ershoff[8] has noted that prolonged pantothenate deprivation leads to a decline in food intake and suggests that forced feeding may help to overcome deprivation-induced symptoms, although he believes that reduced intake alone cannot be adduced as the only factor involved. The present results tend to support his hypothesis along with that of Beznák and van Alphen,[10] who contend that the symptom-poor picture of pantothenate deficiency obtained by recent investigators is due to their use of a uni-deficient diet, while earlier researchers used a multi-deficient diet.

It would probably be a mistake to suppose that the effects of inanition and pantothenate deprivation are additive. The data presently

* A second experiment, this time using chronic rather than acute undernutrition, also demonstrated differential effects due to pantothenic acid deprivation. Statistical tests indicate that these effects are independent of weight and food intake changes.

available[1,3,7,8] indicate that both conditions derange a wide variety of functions and interact in a rather complex fashion. For example, they produce adrenal impairment via two different avenues: hypersecretion of ACTH (inanition) and insufficiency within the adrenals themselves (pantothenate-deficiency). Also, as a component of CoA, pantothenic acid influences the operation of many metabolic processes. The response to pantothenate surfeit, moreover, seems to depend on the general nutritive state of the animal. Dumm and Ralli,[4] using unilateral adrenalectomy as a stress, found that large supplements of pantothenate increased adrenal cholestrol levels in rats fed a 16 per cent protein diet but not in those fed a 22 per cent protein diet. Granados and Verzár,[5] also working with adrenalectomized rats, reported that supplements of pantothenate prolonged survival only if adequate quantities of fat and the B-vitamins were present in the diet. Thus, it seems that the role of pantothenic acid can be defined only as a function of the nutritional status in other respects.

SUMMARY

After preliminary training in the Skinner box, during which they learned to activate a heat lamp by pressing a lever, sixteen albino rats were separated into two equal groups. One was put on a pantothenate-enriched diet (2 mg daily). The other was put on a pantothenate-deficient diet. The frequency of heat-reinforced responses in an ambient temperature of 0° C was recorded for a period of four weeks, during which the animals were in the Skinner box for four hours per week. When differences in response rate did not appear at the end of this time, both groups were submitted to a starvation diet. This resulted in a marked increase in frequency of responding for both groups, with the rate for the pantothenate-deprived group being significantly greater. It was concluded that food and pantothenate-deprived animals are more sensitive to cold than animals deprived only of food.

REFERENCES

1. Ralli, E. P., and Dumm, M. E.: Relation of pantothenic acid to adrenal cortical function. *Vitamins and Hormones* 9: 133, 1953.
2. Casentini, S., Libretti, A., and Tusini, G.: Sul quadro isotochimico e sul contenuto in colesterlo e acido ascorbico dei surreni di animali carenti in acido pantotenico e tratti o no con ACTH. *Arch. Internat. Pharmacodyn. Therap.* 92: 217, 1952.
3. Cowgill, G. R., Winters, R. W., Schultz, R. B., and Krehl, W. A.: Pantothenic acid deficiency and the adrenals: some recent experiments and their interpretation. *Internat. Ztschr. Vitaminforsch.* 23: 275, 1952.
4. Dumm, M. E., and Ralli, E. P.: Influence of ascorbic acid, pantothenic acid and protein on the resynthesis of adrenal cholesterol after stress. *Fed. Proc.* 13: 38, 1954.
5. Granados, H., and Verzár, F.: The influence of pantothenic acid and other B-vitamins on the adrenalectomized rat. *Internat. Ztschr. Vitaminforsch.* 24: 403, 1952.
6. Beare, J. L., Beaton, J. R., and McHenry, E. W.: Anterior pituitary growth hormone administration in B vitamin deficiencies in the rat. *Endocrinology* 55: 40, 1954.
7. Novelli, G. D.: Metabolic functions of pantothenic acid. *Physiol. Rev.* 33: 525, 1953.
8. Ershoff, B. H.: Comparative effects of pantothenic acid deficiency and inanition on resistance to cold stress in the rat. *J. Nutrition* 49: 373, 1953.
9. Skinner, B. F.: *The Behavior of Organisms.* Appleton-Century-Crofts, New York, 1938.
10. Beznák, A. B. L., and van Alphen, G. W. H. M.: Cardiac automatism and choline acetylation in rats on thiamine and pantothenic-acid-deficient diets. *Canad. J. Biochem. Physiol.* 33: 867, 1955.

Physical Performance Capacity and Nutriture: Evaluation of Rations by Animal Experimentation

By D. R. YOUNG, PH.D. AND HARRY SPECTOR, PH.D.

NUTRITION research was at first largely concerned with measurement of energy metabolism, determination of the essential nutrients, and delineation of the syndromes resulting from specific nutrient deficiencies. These studies emphasized such criteria as changes in growth, reproduction, lactation, gross and tissue pathology. It has been amply demonstrated in these investigations that nutritional deficiencies adversely affect a large number of tissues in the body—the effects varying in degree and in kind with the individual tissue[1] from simple alterations in chemical composition to profound morphologic changes. Other investigations indicated that nutritional inadequacies resulting either from dietary deficiencies or conditioned malnutrition may in many cases become more manifest as changes in physical performance or as alterations in the biochemical and physiologic responses to work stresses.[2]

That performance is the ultimate criterion of physical fitness is axiomatic. It is logical, therefore, that the attention of the nutritionist has been directed to the influence of nutrition on work capacity. Theoretical considerations led some enthusiasts to pursue the hope that a special state of robust health and "superman" performance capacity could be achieved by special diets, particularly those abundant in the vitamins and the "ergogens".[3] While research has exploded this idea it has undeniably demonstrated that deficiency of any essential nutrient results sooner or later in physical deterioration. But how low the dietary intake of specific nutrients can be without evidence of deterioration in the ability to do work is still unsettled. This situation has resulted in part from difficulties in objective measurement of performance in man: human performance is conspicuously dependent on motivation, and long training periods may be required in order to establish a reasonably stable level of skilled performance.

Nowhere is the premium on maximum performance greater than in military personnel of the modern army. In the last analysis, its efficiency is determined by the ability of individual men to perform assigned missions. In order to design and develop rations which will maintain the performance capacity of the human engine at a level essential to realization of a full military potential, it is important to utilize criteria of military significance for the evaluation of the nutritional adequacy of combat rations. Physical performance capacity has obvious appeal as such a criterion. Maximum utilization of this criterion in military ration development requires that tests be developed which take advantage of the speed, economy, and rigor of control of animal experimentation.[4]

The purpose of this paper is to review critically the methods available for the measure-

From the Quartermaster Food and Container Institute for the Armed Forces, Chicago, Illinois. This paper has been assigned number 640 in the series of papers approved for publication. The views or conclusions contained in this report are those of the authors. They are not to be construed as necessarily reflecting the views or endorsement of the Department of Defense.

Presented at a Symposium on Nutrition and Behavior held at the Laboratory of Physiological Hygiene, University of Minnesota, April 27, 1956, with the cooperation of the National Vitamin Foundation, Inc., New York and under the sponsorship of the School of Public Health, University of Minnesota.

ment of physical performance capacity in man and animals, to examine briefly the literature on the relationship of diet to performance, and finally to appraise the potential for developing suitable technics for measurement of physical performance capacity of animals as a criterion of nutritional adequacy of the diet.

PERFORMANCE TESTS IN MAN

The physical performance tests now in use fall into two major categories: (a) direct measurements of performance under standard conditions and (b) indirect tests involving the measurement of physiologic or biochemical changes at the end of, or during recovery from a work task. In the latter type of measurement the work task may be maximal or submaximal. For man the problems of performance analysis with special reference to the impact of nutrition on performance, have been discussed by a number of authors.[5-10] Tests of industrial performance have measured such human abilities as (a) general dexterity of finger, hand-wrist, and arm, (b) dual hand dexterity, (c) bilateral hand dexterity, (d) hand-foot coordination, (e) machine tending ability, and (f) inspection ability. A large number of work situations have been set forth by Brožek and Monke[11] as potential tools for investigating the numerous variables associated with occupational performance.

Much more, however, has been done in the area of strictly physical (non-productive) performance, with procedures and test methods designed to determine either strength or endurance, or both. Coordination of will power, mechanical precision, and the durability of the physiologic and biochemical processes, lend themselves to factor analysis and estimates of the variables involved in the continuous performance of a motor task. Each component of overall fitness is in itself a function of many parameters, of which nutritional effects are but one element. Constitutional type ("body build") has been related by Sheldon[12] to capacity for strenuous physical work and to nutriture by Brožek.[13] Several interrelationships between body composition and physiologic requirements for specialized activities have been set forth by Behnke.[14] Keys, *et al.*[15] found that chronic undernutrition produced marked deterioration in strength, and especially in endurance.

Government agencies have used the "physical fitness" tests with both military and civilian personnel.[16-20] Numerous athletic tests have been evaluated by Cureton, *et al.*[21] The most useful endurance tests have been found to involve rowing, pedalling, step-ups with or without added weights (pack test), weight lifting (bucket test), pulling (stoneboat test), swimming, walking or running, and treadmill running. All can be graded in terms of intensity to permit investigation of the effects of light, heavy, or moderate work. Measurements taken after the completion of light or moderate work have provided much useful information for the general study of the physiology of exercise. However, most of the quantitative relationships between physical fitness and nutritional state have been established by tests that have approached maximal physical performance.

Whereas work tests have been successfully conducted both in the field and in the laboratory, the most successful tests of mental or neuromuscular function have been conducted only in the laboratory, although some useful information pertaining to neuromuscular fitness has been brought to light by field agility testing. The laboratory tests include measures of strength, speed, and coordination and provide data on visual and auditory acuity as well as motor performance. Many of these have been listed by Keys *et al.*[15] and by Brožek and Taylor.[22] The neuromuscular and strictly mental tests will not be discussed here since it is believed that extension of these measures to laboratory animals is in most cases unrewarding due to difficulties in the standardization of such tests and interpretation of results. Moreover, intellective functions are not significantly altered by undernutrition even though the chemical alterations may be severe.[9,10]

Some of the problems of the measurement of fatigue and of exhaustion as an end point of work capacity have been discussed.[23] Fatigue is a resultant of many factors, including training and motivation. Motivation is especially difficult to assess since it is so susceptible to

extrinsic and intrinsic factors, and, according to Carmichael *et al.*[24] in some cases not a continuous function of the duration of work. The effects of training on performance are well known and have been attributed by some exclusively to improved coordination.[25] However, the effects of training and motivation have been minimized in previous work tests where each subject has served as his own control in longitudinal studies, where motivation has been kept at a uniformly high level, and where body responses have been used to supplement performance time and efficiency as criteria of work capacity. Included in these are the measurement of bioelectric potentials of muscles,[24] changes in electrical impedance on the body surface,[26] alterations in the neuromuscular responses to galvanic stimulation,[27] changes in the thresholds of reflexes,[28] and the coagulation reaction of urine.[29] However, of the numerous attempts to relate work intensity to physiologic alteration, the most successful formulations have evolved from cardiovascular and respiratory responses to specific endurance tests. Effects of physical fitness on the physiologic responses to work are noted in Table I.

Extrapolation of respiratory and cardiovascular responses to work of known intensity

TABLE I[30–46]

Effect of Physical Fitness in Man on Physiologic Responses to Work

Level of activity	Index	Relative change* in unfit subjects	Reference
A. At rest	1. Pulse	+	30, 31
	2. Standing diastolic pressure	−	32, 33
	3. Standing systolic pressure	−	32, 34
	4. Pulse pressure	−	32, 34
B. Easy work that can be sustained in the steady state	1. O_2 consumption	+	35
	2. CO_2 production	+	35
	3. R.Q.	+	34
	4. Ventilation	+	36, 37
	5. Respiratory rate during work	+	36
	6. O_2 pulse	−	38
	7. Ventilatory efficiency	−	36
	8. Pulse rate during work	+	35, 39
	9. Pulse rate deceleration after work	−	35, 40
	10. Systolic pressure during work	+	39
	11. Rate of decline of systolic pressure after work	−	39
	12. Cardiac output-stroke volume	−	39, 41
	13. Mechanical efficiency	−	35, 39
	14. Blood lactate during work	+	42, 41
C. Exhausting work that cannot be sustained in the steady state	1. Duration	−	32, 33, 44
	2. Maximal O_2 consumption	−	43, 45
	3. Maximal CO_2 production	−	43
	4. R.Q.	+	35
	5. Maximal ventilation	+	36
	6. Ventilatory efficiency	−	34
	7. Oxygen pulse	−	38
	8. Maximal pulse rate during work	+	38, 45
	9. Pulse rate deceleration after work	−	38, 45
	10. Systolic pressure during work	−	32
	11. Rate of decline of blood pressure after work	−	32
	12. Blood lactate at end of work	−	43
	13. Blood sugar at end of work	−	46
	14. O_2 debt	−	30, 43

* + or − refers to relative increase or decrease as compared to a physically fit subject.

in order to predict work capacity in untried situations is usually complicated by the non-linearity of relationships at high levels of work output. One example is the use of the maximal oxygen consumption as a measure of work capacity: at high levels of work intensity oxygen uptake is relatively constant or begins to decrease while the blood oxygen tension may not be significantly decreased. Moreover, because of the relatively fixed character of vital capacity, maximal ventilation and oxygen consumption may be only rough approximations of work capacity. Breath holding, which measures relative sensitivity to both low blood pO_2 and pCO_2, has also been proposed as a test of physical endurance. If a maximal value is desirable, recovery oxygen uptake may be a more rewarding criterion. On theoretical grounds there is also merit in using the blood lactate level in conjunction with respiratory data as a measure of performance capacity since its appearance in the blood in excessive quantities corresponds to a work output approximating two-thirds of the maximal.

Attempts to predict working capacity from cardiovascular responses to work have employed the relative changes in pulse rate and blood pressure, the recovery pulse rate, and a combination of blood lactate and blood pressure. Using these criteria, problems of fitness scoring frequently arise from the fact that for a given physical work intensity the maximal pulse will never be as high during certain types of malnutrition—due to concomitant bradycardia—as is found with normal dietary conditions.

PERFORMANCE TESTS IN ANIMALS

Three general methods of studying activity in experimental animals have been used: (a) artificial stimulation of perfused muscles, (b) measurements of voluntary activity, and (c) measurements of forced activity of the whole animal.

Artificial stimulation of muscles by the usual laboratory technics offers a method of successfully reproducing muscular activity, the advantage of careful control of extrinsic factors, and the possibility of obtaining precise measurements. However, it is difficult from the results obtained to predict causal factors which would limit muscular activity in the whole animal or to quantitatively extrapolate the measured activity to the physical capacity of the intact animal. In anesthetized animals numerous attempts have been made to evaluate the work done by artificially stimulated muscles in terms of the increased whole animal oxygen consumption invoked by the method. Despite stimulation of a diffuse area, whole animal oxygen intake has seldom been raised to a level higher than five times the basal rate. This intensity corresponds to steady state work and is unsatisfactory for evaluating nutritional effects on work performance. However, since the findings of Heron *et al.*[47] that intact muscles of anesthetized rats could contract continually for ten days, the method has been used extensively with a large variety of animals to study the biochemistry of muscular training, to assay endocrine function, and to study the metabolism of muscles and other tissues.[48–53] Recently Levine *et al.*[54] have used the method with rats and dogs to demonstrate that local vascular incompetence is of major importance in the onset of muscular fatigue.

Voluntary activity of animals has been used more extensively to provide information on physical performance, and has also provided measures of learning, drives, and aggressiveness. Three general technics have been used for quantifying voluntary activity; these employ (a) running drums (b) specially mounted cages from which diffuse activity is recorded, or (c) strictly observational measurements.

Of these three methods the revolving drum has been the most extensively used laboratory apparatus for investigating activity.[55,56] Depending upon the experiment, the animal may live entirely within the drum, have a separate living cage, or have access to supplemental diffuse activity cages.[57–63] The usual method of recording running activity has been by means of a counter which records the number of revolutions, thus measuring total activity. Skinner,[64] however, realizing the limitation of this measurement, used a Harvard work-adder attached to a writing lever which recorded activity on a kymograph—the slope

of the line providing a measure of activity as a function of time.

With respect to diffuse activity, Szymanski[65,66] has described a spring mounted cage in which any movement of the cage due to animal activity actuates a recording system. The disadvantage of lack of damping encountered in the spring mechanism has been somewhat overcome by the tambour-mounted activity cages.[67] Measurements of diffuse activity include recordings of the activity of new born children, of chicks, and of monkeys.[68–70] Numerous modifications of this technic which provide greater sensitivity and improved precision have been discussed by others.[71–77] Along these lines Richter and Hines[78] have described a kinesthesiometer for monkeys in which the animal was attached by a chain to a rod—any movement of the rod activated a counter.

Additional measures of voluntary activity include the use of a tilt box in which movement of the animal from one end to another advances a counter or activates a photoelectric relay connected to a counter;[79,80] the use of a horizontal turntable from which activity can be measured either photographically or with a suitable recording device;[81] and the use of a pedometer which has been employed to record gross activity in the sheep and pig and head shaking in chickens.[82,83]

Purely observational means of measuring voluntary activity have been used by Beach,[84] Hall,[85] and Fredericson[86] who recorded either the time required or the behavioral pattern of rats while traversing a prescribed distance. Numerous maze studies reported in the literature will not be discussed here, since the primary purpose of these tests is to investigate learning and animal drives with only secondary attention being paid to work performance.

The most successful tests of *forced activity* in animals have been swimming tests for rats and dogs, treadmill tests for dogs, and work wheel tests for rats and mice.[87–97] Unfortunately many of the voluntary and forced activity measures mentioned above have been classified under the general term "animal activity." This failure to distinguish types of activity in terms of its measure has led to false concepts. Animal activity does not constitute a single behavioral category which can be measured with any single instrument, but must be considered for the present in terms of its method of measurement.

Several biologic and physical variables are known to contribute to intra-animal and intergroup variability. One is the difficulty in estimating the overall intensity of the work test. Although swimming to exhaustion offers the advantage of obtaining a reproducible endpoint, swimming time in both rats and dogs is markedly affected by water temperature. Both high- and low-water temperatures decrease swimming capacity; these effects are related to the inability of the animal to maintain body temperature under extreme conditions.[98,99] In addition, work capacity might be limited by hyperventilation (panting for evaporative cooling) and the resulting alkalosis brought about by high water temperatures. It has been reported that the rat can swim as long as 48 hours at comfortable water temperatures; this period is obviously too long for a useful measurement of specific nutritional defects.

Although running tests have been satisfactorily conducted with dogs and larger animals, the use of work wheels and treadmills for rodents is limited. While reports have indicated that rats will voluntarily run a distance of 5 to 15 miles per day, forced activity at this rate has in many cases induced mortality indicating that factors other than muscular activity are involved.

Intrinsic as well as extrinsic factors contribute to the variability in results of voluntary activity tests. These factors include heredity, age, hunger, external environment, endocrine imbalance, and activity following confinement. Although uniformly high correlation coefficients for voluntary activity under specified conditions have been reported, it is believed that this is merely a reflection of the consistency of the equipment and fortunate selection of animals. This belief is strengthened by consideration of reports that rats in larger wheels run farther than those in smaller wheels, that within litter-mates some rats run only 200 revolutions per day and others as much as

2000, and that the number of revolutions per day are reduced when the rat is presented with a choice of physical distraction.[62] In addition, special consideration must be given to the fact that factors which influence diffuse activity in one direction may affect running activity in another direction.

By selective breeding Rundquist[100] has been able to get active and inactive breeds of rats, and although the daily activity periods were determined by the internal rhythm of the animal, the genetic factors could be obscured by certain environmental influences especially light and darkness. In this respect Browman[101,103] and Johnson[104] have been able to alter the daily activity rhythm of small animals by changes in light intensity. The reported effects of environmental temperature on voluntary activity have not been consistent. In young (poikilothermic) mice Stier[105] has found that the rate of activity is a function of body temperature and of several other factors, including quiescence and frequency of activity. More recently Jones *et al.*[106] have reported that when environmental conditions of temperature, light, and sound are controlled, activity of normal male rats in wheel cages is a function of the animal's experience in the wheel and age. For animals of equal experience, activity varies inversely with age, while in animals of equal age, activity varies directly with experience. The fact that the relationships are not linear indicates a possible interaction between these two factors affecting activity.

Considered *in toto* the measurement of voluntary activity, despite careful control of environmental factors and in the selection of animals to remove endocrine and genetic effects, leaves much to be desired as a measure of work performance. While such measurements have a recognized value in the study of animal behavior, this approach does not lend itself to a careful evaluation of nutriture. The interested reader is referred to other articles for further reviews on spontaneous activity.[107–111]

DIET AND PERFORMANCE

The literature on the influence of nutrition on work performance has been reviewed by Keys[10] and by Simonson[9] who questioned the reliability of a substantial part of the data because of the failure to define precisely performance uninfluenced by extraneous factors such as environment, training and motivation, and the questionable nature of the criteria used for definition of nutritional states and working capacity. It is our purpose, then, in this section to briefly re-emphasize the need for more exacting control and standardization of type and intensity of work tests, and to extract guiding information on the effect of dietary insufficiency on performance.

Lack of adequate controls and standardization has led frequently to conflicting reports on the effects of either dietary restriction or supplementation on work performance.

TABLE II

Rate of Onset of Deficiency Syndromes in Working Men Exposed to Complete Deficiency of One or More of the Important Nutrients*

Nutrient	Time before earliest deleterious effects appear in complete deficiency	Earliest deficiency syndromes and end results
Water	A few hours	Easy fatigue, poor performance. Eventual exhaustion of dehydration.
Calories	Two or three days	Easy fatigue, poor performance.
Sodium chloride	Several days	Easy fatigue, poor performance. Eventually, heat cramps.
Carbohydrate	Several days	Easy fatigue, poor performance. Eventually, nutritional acidosis.
Vitamin B complex	One or two weeks	Easy fatigue, poor performance. Eventually, one of the B-deficiencies, usually beri-beri.
Vitamin C	Several weeks	Easy fatigue, poor performance. Eventually, scurvy.
Protein	Probably several weeks	Earliest effects not known; late result, nutritional edema.
Vitamin A	Several months	Earliest effects not known.
Fats	Many months	Earliest effects not known.

* From Johnson, R. E.; Nutritional standards for men in tropical climates, *Gastroenterology*, 1: 838, 1943.

TABLE III[87,95,96,115–136]

Some Effects of Diet on Performance in Animals

Nutrient	Dietary treatment	Animal	Type of activity	Effect on activity*	Reference
A. Water	1. Deprivation	Rat	Running†	+	115
B. Minerals	1. Total deprivation	Rat	Running	+	116
	2. Mg deprivation	Rat	Running	−	115
	3. P or Fe deprivation	Rat	Learning	−	117
C. Calories	1. Total deprivation (fasting)‡	Rat	Enforced running	−	96
D. Fat	1. 1–10% fat	Rat, mouse	Swimming at 37° C	0	118
	2. 10% fat	Rat, mouse	Swimming at 20° C	−	118
	3. 40% fat	Rat	Swimming at 32° C	+	119
E. Protein	1. Protein restriction	Rat	Running	−	120
	2. Protein deprivation	Rat	Learning	−	121
	3. Lysine deprivation	Rat	Running	+	122
	4. Supplementation with cystine or glutamic acid	Rat	Learning	0	123
F. Vitamins	Deprivation				
	1. Vitamin A	Rat	Learning	0	124
	2. Thiamine				
	a. Acute	Rat	Running	+	95
	b. Chronic	Rat	Running	−	95
	c. Chronic	Mouse	Aggressiveness	0	125
	3. Thiamine and riboflavin	Rat	Learning	−	126, 127
	4. Thiamine, riboflavin, and nicotinic acid	Rat	Running	0	128
	5. B-complex				
	a. Acute	Rat	Learning	−	129
	b. Chronic	Rat	Running	−	130
	Excess supplementation				
	1. Thiamine	Pigeon	Flying	+	131
	2. B-complex (in perfusion medium)	Frog	Muscle contraction	+	132
G. Miscellaneous "Factors"	Addition of:				
	1. Propylene glycol	Rat	Running	+	133
	2. Diethylene or dipropylene glycol	Rat	Running	−	133
	3. Thyroxine, diiodothyronine, or methylene blue	Dog	Running (treadmill)	0	134, 135
	4. Desiccated liver	Rat	Swimming at 20° C	+	87
	5. Wheat germ oil	Guinea pig	Swimming at 37° C	+	136

* + = increase in activity; − = decrease in activity; 0 = no change in activity.

† Spontaneous running unless otherwise indicated.

‡ Decrease in running was influenced by the previous diet in the following order: Fat < Carbohydrate <Protein.

Thus, effects of a given dietary treatment as measured by moderate (steady-state) work may be unlike those obtained by measures of heavy work of relatively short duration. Bicycle ergometer tests and treadmill tests may elicit significantly different responses.[112,113] In past considerations of these methods, it has been argued that one measures endurance and coordination while the other measures endurance and strength. It is en-

tirely possible that the requirements for one do not necessarily reflect the immediate needs of the other.

Bearing in mind the various factors involved in nutritional deficiencies, what sort of picture may be drawn of the course of events which may be expected to occur as the deficient state develops? Current knowledge is inadequate to establish precisely the pattern of deterioration in fitness. For general guidance a chart was developed by Johnson[114] and is reproduced here as Table II. It can be seen that easy fatigue and poor performance are generally amongst the earliest deleterious effects to appear in working men exposed to complete deficiency of an essential nutrient.

Some relationships between diet and animal performance are set forth in Table III.

EVALUATION OF POTENTIAL OF MEASURING NUTRITIONAL ADEQUACY OF RATIONS BY PERFORMANCE IN ANIMALS

What loss in operational efficiency may result from drastic dietary changes? It is particularly germane to ask if populations adapted to a normally *luxus* consumption of nutrients would suffer a significant loss in performance capacity if the diet were abruptly altered and limited.

When is the deterioration of performance likely to reach serious proportions if the dietary deficiency continues unabated? Why does the ability to do physical work fall off at different rates with different nutrient deficiencies? And conversely, why does rate of recovery of ability to perform vary with the nutrient which has been depleted?

It is believed that animal studies offer many advantages for the development of basic data which will provide the answers to these important questions. Desired test methods are those which impose a measurable and recognized strain on the animal. Severity should be sufficiently flexible to permit investigation not only of acute "all-out" effort, but submaximal work sustained for prolonged periods. Equipment and procedures should be versatile enough to permit investigations of the effects of environment superimposed on dietary and work stress. A review of the literature reveals two promising methods: (a) swimming and (b) running.

Comprehensive test systems should include measurements of performance of the body as a whole as well as the function of component parts; and data should discriminate between the variables under consideration, predict deterioration, and establish the time-factor relationships in recovery or return to physiologic "normalcy." The promising tests which reflect the physical strain and the biochemical distortions include measurements of: (a) endocrine function (thyroid, adrenal), (b) liver function (serum cholinesterase), (c) kidney function (clearance, pre-formed elements), (d) nutrient balance, (e) cardiovascular responses (cardiac output, pulse rate, blood pressure), (f) respiratory changes (maximal oxygen consumption, O_2 debt, blood buffers), and (g) blood chemistry (blood sugar, lactate, pyruvate). These measurements have been found to reflect the insults of water and caloric deficits. Little information however, is available regarding the immediate and long range effects of protein, fat, vitamin, and mineral insufficiency which can be interpreted by current clinical thought. For this purpose long observational periods of severe physical exertion are needed; carcass and organ analyses provide important data for explaining the observed functional changes. It is in this area that animal tests are particularly useful.

REFERENCES

1. Follis, R. H.: *The Pathology of Nutritional Disease.* Charles C Thomas, Springfield, Ill., 1948.
2. *Modern Nutrition in Health and Disease.* Edited by M. G. Wohl and R. S. Goodhart, Lea and Febiger, Philadelphia, 1955, Chapter 36.
3. Phipson, E. S.: Doping in athletic contests. *Indian Med. Gaz.* 75: 484, 1940.
4. Brožek, J.: Nutrition and performance in animals in *Method for Evaluation of Nutritional Adequacy and Status.* National Research Council, Washington, D. C., December 1954, p. 155.
5. Brožek, J.: Psychological factors in relation to performance and fatigue. *Fed. Proc.* 2: 134, 1943.
6. Morell, T.: Combat of fatigue by active substances. *Bull. War Med.* 2: 420, 1941–42.
7. Herlitzka, A.: Physiology of human work. *Science* 107: 282, 1948.
8. Dill, D. B., Bock, A. V., Edwards, H. T., and Kennedy, P. H.: Industrial fatigue. *J. Indust. Hygiene* 18: 417, 1936.

9. SIMONSON, E.: Influence of nutrition on work performance. *Nutrition Fronts in Public Health* No. 3, p. 72, 1951.
10. KEYS, A.: Physical performance in relation to diet. *Fed. Proc.* 2: 164, 1943.
11. BROŽEK, J., and MONKE, J. V.: Miniature work situations as a research tool. *Indust. Hyg. and Occ. Med.* 2: 63, 1950.
12. SHELDON, W. H., STEVENS, S. S., and TUCKER, W. B.: *The Varieties of Human Physique.* Harper and Bros., New York, 1940.
13. BROŽEK, J.: Measuring nutriture. *Am. J. Phys. Anthrop.* 11: 147, 1953.
14. BEHNKE, A. R.: Physiologic studies pertaining to deep sea diving and aviation especially in relation to fat content and composition of the human body. *Harvey Lectures* 37: 198, 1942.
15. KEYS, A., BROŽEK, J., HENSCHEL, A., MICKELSON, O., and TAYLOR, H. L.: *The Biology of Human Starvation.* Vol. 2. The University of Minnesota Press, Minneapolis, 1950.
16. Bureau of Naval Personnel. *Physical fitness manual for the U. S. Navy*, p. 17. Training Division, Physical Fitness Section, Washington, D. C., 1943.
17. Federal Security Agency. *Physical fitness through physical education for the victory corps*, p. 80. U. S. Office of Education, Washington, D. C., 1942.
18. Federal Security Agency. *Physical fitness of students in colleges and universities*, No. 3, p. 58. U.S. Office of Education, Washington, D. C., 1943.
19. STANSBURY, E. B.: The physical fitness program of the Army Air Force. *J. Health and Phys. Educ.* 14: 463, 1943.
20. BANK, T. P.: The Army physical conditioning program. *J. Health and Phys. Educ.* 14: 195, 1943.
21. CURETON, T. K., HUFFMAN, W. J., WELSER, L., KIREILIS, R. W., and LATHAM, D. E.: Endurance of young men. *Monog. Soc. Res. Child Develop.* Vol. 10, 1945.
22. BROŽEK, J., and TAYLOR, H. L.: Tests of motor functions in investigations of fitness. *Am. J. Psychol.* 67: 590, 1954.
23. FORBES, W. H.: Problems arising in the study of fatigue. *Psychosomatic Med.* 5: 155, 1943.
24. CARMICHAEL, L., KENNEDY, J. L., and MEAD, L. C.: Some recent approaches to the experimental study of human fatigue. *Science* 110: 445, 1949.
25. STEINHAUS, A. H.: Physiology of movement and measures of coordination. *J. Health Phys. Educ.* 3: 44, 1932.
26. ELBEL, E. R., and RANKIN, R. R.: Palmer skin resistance as a measure of physical fitness. *Am. J. Physiol.* 147: 1, 1946.
27. BEEBE, G. W.: Medical evaluation of nutritional status. *Milbank Mem. Fund Quart.* 21:311, 1943.
28. QUO, SUNG-KER.: A new method of measuring fatigue by the threshold stimulus of the Achilles Tendon reflex. *J. Appl. Physiol.* 2: 148, 1949.
29. TAKANO, S.: The nature of the coagulation reaction of copper ferrocyanide colloid solution. *Science* 21: 297, 1951.
30. KNEHR, C. A., DILL, D. B., and NEUFELD, W.: Training and its effects on man at rest and at work. *Am. J. Physiol.* 136: 148, 1942.
31. PROSCH, F.: The effect of exercise on heart rate. *Research Quart.* 4: 75, 1932.
32. DAWSON, P.: *The Physiology of Physical Education*, Baltimore Press, Baltimore, 1935.
33. SCHNEIDER, E. C.: *Physiology of Muscular Activity.* W. B. Saunders, Philadelphia, 1939.
34. STEINHAUS, A. H.: Chronic effects of exercise *Physiol. Rev.* 13: 103, 1933.
35. DILL, D. B., TALBOTT, J. H., and EDWARDS, H. T.: Studies in muscular activity. *J. Physiol.* 69: 267, 1930.
36. BRIGGS, H.: Physical exertion, fitness, and breathing. *J. Physiol.* 54: 292, 1920.
37. TAYLOR, C.: Studies in exercise physiology. *Am. J. Physiol.* 135: 27, 1941.
38. SCHNEIDER, E. C., and CRAMPTON, C. B.: Comparison of some respiratory and circulatory reactions of athletes and non-athletes. *Am. J. Physiol.* 129: 165, 1940.
39. BOCK, A. V., VAN CAULAERT, C., DILL, D. B., FOLLING, A., and HURXTHAL, L. M.: Studies in muscular activity. III. Dynamical changes occurring in man at work. *J. Physiol.* 66: 136, 1928.
40. DILL, D. B., and BROUHA, L.: Studies on heart rhythm during exercise. *Travail Humain* 5: 1, 1937.
41. DILL, D. B.: The economy of muscular exercise. *Physiol. Rev.* 16: 263, 1936.
42. EDWARDS, H. T., BROUHA, L., and JOHNSON, R. E.: Effects of training on blood lactic acid during muscular work. *Travail Humain* 8: 1, 1940.
43. ROBINSON, S., and HARMON, P. M.: The lactic mechanism and certain properties of the blood in relation to training. *Am. J. Physiol.* 132: 757, 1941.
44. BAINBRIDGE, F. A.: *The Physiology of Muscular Exercise.* Longmans Green, New York, 1931.
45. ROBINSON, S., EDWARDS, H. T., and DILL, D. B.: New records in human power. *Science* 85: 409, 1937.
46. ROBINSON, S.: Experimental studies of physical fitness in relation to age. *Arbeitsphysiologie* 10: 251, 1938.
47. HERON, W. T., INGLE, D. J., and HALES, W. M.: Work output of rats subjected to continuous faradic stimulation. *Science* 76: 550, 1932.
48. FLOCK, E. V., INGLE, D. J., and BOLLMAN, J. L.: Formation of lactic acid, and initial process in working muscle. *J. Biol. Chem.* 129: 99, 1939.
49. GOLDSTEIN, M. D., MULLICK, V., HUDDLESTON, B., and LEVINE, R.: Action of muscular work on transfer of sugars across cell barriers:

Comparison with action of insulin. *Am. J. Physiol.* 173: 212, 1953.

50. INGLE, D. J., TORRALBA, G., and FLORES, V.: Comparative effects of muscle work and insulin upon plasma amino acids in eviscerated rats. *Proc. Soc. Exp. Biol. & Med.* 89: 625, 1955.
51. FORSGREN, E.: The relation between liver glycogen and muscular work. *Nord. med.* 3: 2859, 1939.
52. PALLADIN, A. V.: The biochemistry of muscle training. *Science* 102: 576, 1945.
53. EMBDEN, G., and HABS, H.: Chemical and biological changes in muscles after repeated faradic stimulation. *Ztschr. Physiol. Chem.* 171: 16, 1927.
54. LEVINE, R., GOLDSTEIN, M. S., and RAMEY, E. R.: Studies on the mode of action of cortisone in stress situations. *Bull. New England Med. Center* 13: 114, 1951.
55. STEWART, C. C.: Variations in daily activity produced by alcohol and by changes in barometric pressure and diet with a description of recording methods. *Am. J. Physiol.* 1: 40, 1898.
56. SLONAKER, J. R.: Description of apparatus for recording the activities of small animals. *Anat. Rec.* 2: 116, 1908.
57. SHIRLEY, M.: Studies in activity. I. The consistency of the revolving drum method of measuring the activity of the rat. *J. Comp. Psychol.* 8: 23, 1928.
58. SHIRLEY, M.: Studies in activity. II. Activity rhythms, age and activity, activity after rest. *J. Comp. Psychol.* 8: 159, 1928.
59. SLONAKER, J. R.: The normal activity of the white rat of different ages. *J. Comp. Neurol. Psychol.* 17: 342, 1907.
60. PARK, O., and WOODS, L. P.: A modified Hemmingsen-Krarup mammalian activity recorder. *Proc. Soc. Exp. Biol. & Med.* 43: 366, 1940.
61. RICHTER, C. P.: A behavioristic study of the activity of the rat. *Comp. Psychol. Monogr.* 1: 1, 1922.
62. RICHTER, C. P.: Animal behavior and internal drives. *Quart. Rev. Biol.* 2: 307, 1927.
63. RICHTER, C. P.: Contributions of psychology to the understanding of problems of personality and behavior. IV. Biological foundations of personality differences. *Am. J. Orthopsychiat.* 2: 345, 1932.
64 SKINNER, B. F.: The measurement of spontaneous activity. *J. Gen. Psychol.* 9: 3, 1933.
65. SZYMANSKI, J. S.: A method for the investigation of rest and activity periods in animals. *Arch. ges. Physiol.* 158: 343, 1914.
66. SZYMANSKI, J. S.: Activity and rest in animals and humans. *Zeitschr. allg. Physiol.* 18: 105, 1920.
67. SMITH, K. U.: An accurate method of recording activity in animals. *J. Gen. Psychol.* 27: 355, 1942.
68. IRWIN, O. C.: Effect of strong light on the body activity of newborns. *J. Comp. Psychol.* 32: 233, 1941.
69. WILBUR, K. M.: A method for the measurement of activity of small animals. *Science* 84: 274, 1936.
70. KENNARD, M. A., SPENSER, S., and FOUNTAIN, G.: Hyperactivity in monkeys following lesions of the frontal lobes. *J. Neurophysiol.* 4: 512, 1941.
71. SCOTT, C. C., and WORTH, H. M.: An improved device for recording activity of rats. *Proc. Soc. Exp. Biol. & Med.* 66: 285, 1947.
72. SCHULTE, J. W., TAINTER, M. L., and DILLE, J. M.: Comparison of different types of central stimulation from analeptics. *Proc. Soc. Exp. Biol. & Med.* 42: 242, 1939.
73. HARNED, B. K., CUNNINGHAM, R. W., and GILL, E. R.: An activity analyzer for small animals. *Science* 116: 369, 1952.
74. RICHARDS, T. W.: An inexpensive apparatus for the measurement of bodily activity. *Science* 81: 568, 1935.
75. WATERMAN, F. A.: A kinesimeter for studying the spontaneous activity of small animals. *Science* 106: 499, 1947.
76. CAMPBELL, C. J., and MCLEAN, R. A.: An electronic integrating circuit for recording the spontaneous activity of animals. *Rev. Scient. Instruments* 19: 808, 1948.
77. CASTANERA, T. J., KIMELDORF, D. J., and JONES, D. C.: An apparatus for measurement of activity in small animals. *J. Lab. & Clin. Med.* 45: 825, 1955.
78. RICHTER, C. P., and HINES, M.: Increased spontaneous activity produced in monkeys by brain lesions. *Brain* 61: 1, 1938.
79. BOUSFIELD, W. A., and MOTE, F. A.: The construction of a tilting activity cage. *J. Exp. Psychol.* 32: 450, 1943.
80. SIEGEL, P. S.: A simple electronic device for the measurement of the gross bodily activity of small animals. *J. Psychol.* 21: 227, 1946.
81. FARRIS, E. J., and ENGVALL, G.: Turntable for exercising rats. *Science* 90: 144, 1939.
82. CURTIS, Q. F.: Diurnal variations in the free activity of sheep and pig. *Proc. Soc. Exp. Biol. & Med.* 35: 566, 1937.
83. LEVY, D. M.: On the problems of movement restraint, tics, stereotyped movements, hyperactivity. *Am. J. Orthopsychiat.* 14: 644, 1944.
84. BEACH, F. A.: Effects of lesions to corpus striatum upon spontaneous activity of the male rat. *J. Neurophysiol.* 4: 191, 1941.
85. HALL, C. S.: Emotional behavior in the rat. III. The relationship between emotionality and ambulatory activity. *J. Comp. Psychol.* 22: 345, 1936.
86. FREDERICSON, E.: The theory of psychomotion as applied to a study of temperament. *J. Comp. Psychol.* 39: 77, 1946.

87. ERSHOFF, B. H.: Beneficial effect of liver feeding on swimming capacity of rats in cold water. *Proc. Soc. Exp. Biol. & Med.* 77: 488, 1951.

88. KIMELDORF, D. J., and JONES, D. C.: The relationship of radiation dose to lethality among exercised animals exposed to roentgen rays. *Am. J. Physiol.* 167: 626, 1951.

89. HARRIS, R. E., and INGLE, D. J.: The capacity of vigorous muscular activity of normal rats and of rats after removal of the adrenal medulla. *Am. J. Physiol.* 130: 151, 1940.

90. RICE, H. A., and STEINHAUS, A. H.: Studies in the physiology of exercise. V. Acid-base changes in the serum of exercised dogs. *Am. J. Physiol.* 96: 529, 1931.

91. SCHULTZ, F. W., and MORSE, M.: Factors influencing the serum bicarbonate concentration of the dog during treadmill exercise. *Am. J. Physiol.* 122: 105, 1938.

92. SCHULTZ, F. W., and MORSE, M.: Factors influencing the concentration of the serum protein, chloride, and total fixed base of dog. *Am. J. Physiol.* 121: 293, 1938.

93. HASTINGS, A. B.: An investigation of changes in the blood and urine resulting from fatigue. *Public Health Rep.* 34: 1682, 1919.

94. CAMPOS, F. A., CONNOR, W. B., LUNDIN, H., and WALKER, T. T.: Some conditions affecting the capacity for prolonged muscular work. *Am. J. Physiol.* 87: 680, 1929.

95. GUERRANT, N. B., and DUTCHER, R. A.: The influence of exercise on the growing rat in the presence and absence of vitamin B_1. *J. Nutrition* 20: 589, 1940.

96. SAMUELS, L. T., GILMORE, R. C., and REINECKE, R. M.: The effect of previous diet on the ability of animals to do work during subsequent fasting. *J. Nutrition* 36: 639, 1948.

97. HART, J. S.: Use of daily metabolic periodicities as a measure of the energy expended by voluntary activity of mice. *Canad. J. Zool.* 30: 83, 1952.

98. TAN, E. M., HANSON, M. E., and RICHTER, C. P.: Swimming time of rats with relation to water temperature. *Fed. Proc.* 13: 150, 1954.

99. DUREUIL, M., and RATSIMANGA, A. R.: Effect of sudden variations in temperature on the capacity for forced work of the normal rat. *Compt. rend. Soc. de Biol.* 142: 70, 1948.

100. RUNDQUIST, E. A.: Inheritance of spontaneous activity in rats. *J. Comp. Psychol.* 16: 415, 1933.

101. BROWMAN, L. G.: Light in its relation to activity and estrous rhythms in the albino rat. *J. Exp. Zool.* 75: 375, 1937.

102. BROWMAN, L. G.: The effect of controlled temperatures upon the spontaneous activity rhythms of the albino rat. *J. Exp. Zool.* 94: 477, 1943.

103. BROWMAN, L. G.: Modified spontaneous activity rhythms in rats. *Am. J. Physiol.* 142: 633, 1944.

104. JOHNSON, M. S.: Effect of continuous light on periodic spontaneous activity of white-footed mice. *J. Exp. Zool.* 82: 315, 1939.

105. STIER, T. J. B.: Spontaneous activity of mice. *J. Gen. Psychol.* 4: 67, 1930.

106. JONES, D. C., KIMELDORF, D. J., RUBADEAU, D. O., and CASTANERA, T. J.: Relationships between volitional activity and age in the male rat. *Am. J. Physiol.* 172: 109, 1953.

107. SHIRLEY, M.: Spontaneous activity. *Psychol. Bull.* 26: 341, 1929.

108. MUNN, N. L.: *An Introduction to Animal Psychology.* Houghton Mifflin Co., New York, 1933.

109. MORGAN, C. T.: *Physiological Psychology.* McGraw-Hill Co., New York, 1943.

110. HALL, C. S.: Emotional behavior in the rat. III. The relationship between emotionality and ambulatory activity. *J. Comp. Psychol.* 22: 345, 1936.

111. HOSKINS, R. G.: Studies on vigor. XVI. Endocrine factors in vigor. *Endocrinology* 11: 97, 1927.

112. HENSCHEL, A., TAYLOR, H. L., BROŽEK, J., MICKELSEN, O., and KEYS, A.: Vitamin C and ability to work in hot environments. *Am. J. Trop. Med.* 24: 259, 1944.

113. HOITINK, A. W. J. H.: Inquiries into the influence of work and of the administration of Vitamin C on the human organism. *Biol. Abstracts* 23: 14461, 1949.

114. JOHNSON, R. E.: Nutritional standards for men in tropical climates. *Gastroenterology* 1: 838, 1943.

115. WALD, G., and JACKSON, B.: Activity and nutritional deprivation. *Proc. Nat. Acad. Science* 30: 255, 1944.

116. SMITH, P. K., and SMITH, A. H.: The effect of a diet low in inorganic constituents on the voluntary activity of the albino rat. *Abstr. Proc. Am. Physiol. Soc.* 1934.

117. BERNHARDT, K. S.: Phosphorus and iron deficiencies and learning in the rat. *J. Comp. Psychol.* 22: 273, 1936.

118. ERSHOFF, B. H.: Beneficial effect of low fat diets on the swimming performance of rats and mice in cold water. *J. Nutrition* 53: 439, 1954.

119. SCHEER, B. T., DORST, S., CODIE, J. F., and SOULE, D. F.: Physical capacity of rats in relation to energy and fat content of the diet. *Am. J. Physiol.* 149: 194, 1947.

120. SLONAKER, J. R.: Effects of different per cent of protein in the diet. II. Spontaneous activity. *Am. J. Physiol.* 96: 557, 1931.

121. BERNHARDT, K. S.: Protein deficiency and learning in rats. *J. Comp. Psychol.* 22: 269, 1936.

122. BEVAN, W., LEWIS, G. T., BLOOM, W. T., and ABESS, A. T.: Spontaneous activity in rats fed an amino acid deficient diet. *Am. J. Physiol.* 163: 104, 1950.

123. PILGRIM, F. J., ZABARENKO, L. M., and PATTON, R. A.: The role of amino acid supplementation and dietary protein level in serial learning performance of rats. *J. Comp. and Physiol. Psychol.* 44: 26, 1951.

124. BERNHARDT, K. S.: Vitamin A deficiency and learning in the rat. *J. Comp. Psychol.* 22: 269, 1936.

125. BEEMAN, E. A., and ALLEE, W. C.: Some effects of thiamine on the winning of social contacts in mice. *Physiol. Zool.* 18: 195, 1945.

126. MAURER, S.: The effect of early depletion of vitamin B_2 upon performance in rats. *J. Comp. Psychol.* 20: 385, 1935.

127. MAURER, S.: The effects of partial depletion of vitamin B (B_1) upon performance in rats. *J. Comp. Psychol.* 20: 309, 1935.

128. RICHTER, C. P., and BARELARE, B.: Further observations on the carbohydrate, fat, and protein appetite of vitamin B deficient rats. *Am. J. Physiol.* 127: 199, 1939.

129. BERNHARDT, K. S., and HERBERT, R.: A further study of vitamin B deficiency and learning with rats. *J. Comp. Psychol.* 24: 263, 1937.

130. JAKWAY, I.: Voluntary activity in the rat as related to intake of whole yeast. *J. Comp. Psychol.* 26: 157, 1938.

131. MOURIQUAND, G., and COISNARD, J.: Muscular activity and vestibular chronaxie in normal pigeons. *Compt. rend. Soc. de Biol.* 136: 812, 1942.

132. SHOCK, N. W., and SEBRELL, W. H.: Effect of riboflavin and other B complex vitamins on work of perfused frog muscles. *Proc. Soc. Exp. Biol. & Med.* 63: 290, 1946.

133. VAN WINKLE, W., and KENNEDY, N. K.: Voluntary running activity of rats fed propylene glycol and other glycols. *J. Pharmacol. Exp. Therap.* 69: 140, 1940.

134. GUILD, R., and RAPPORT, D.: Calorigenic action of methylene blue during muscular exercise. *Proc. Soc. Exp. Biol. & Med.* 34: 459, 1936.

135. CANZANELLI, A., SEGAL, M., and RAPPORT, D.: The utilization of the calorigenic action of diiodothyronine and thyroxine in muscular exercise. *Am. J. Physiol.* 110: 410, 1934.

136. ERSHOFF, H., and LEVIN, E.: Beneficial effect of an unidentified factor in wheat germ oil on the swimming performance of guinea pigs. *Fed. Proc.* 14: 431, 1955.

Hunger and Appetite

LAST YEAR at one of the Macy Conferences in Princeton at which Dr. Fremont-Smith encourages interruptions at all times, the main speaker of the day in his first few sentences used a word that someone wanted defined. This started off a discussion and argument that lasted over half of the day.

Today we could easily get into a similar discussion about the two words, "hunger" and "appetite," and something would undoubtedly be gained by a few definitions, but the time is too short. Yet it is well to keep in mind that the speakers may not all be using these terms in the same sense. The topic of this section is concerned in one way or another with an important aspect of behavior of animals and human beings—the taking of nourishment. How much attention *should* be paid in feeding animals and ourselves to the sensation of hunger and to appetite? There are at least three different points of view:

The first is represented by individuals who believe that much attention should be paid to hunger and voluntary dietary selection or appetite; that these are safe and reliable guides to the satisfying of dietary requirements. These individuals believe that beneficial selections of food-stuffs are largely made on the basis of taste—that, when needed, food-stuffs have an attractive taste; when not needed, an unattractive taste; that sensations of satiety are reliable in telling when to stop eating.

The second point of view is represented by individuals who likewise think that animals and human beings are capable of regulating their dietary needs but that they do so on the basis of sensations experienced after the ingestion of food-stuffs, which involves a conditioning process.

The third point of view is represented by individuals who do not believe that animals or human beings are capable of regulating their dietary needs on the basis of any sensation of hunger or appetite; they believe that diets must be prescribed, that we must be told when to eat, and how much. The representatives of this view pay little attention to the taste of food-stuffs or the sensations derived from their ingestion; they may go so far in eliminating any possible regulation through taste as to recommend giving food-stuffs in capsules.

Our speakers may throw light on the validity of one or the other of these viewpoints.

CURT P. RICHTER, PH.D.
The Johns Hopkins Hospital
Baltimore, Md.

Taste Mechanisms in Preference Behavior

By CARL PFAFFMANN, PH.D.*

I SHOULD like to preface my remarks with some general considerations on the chemical senses. Sensory psychologists and physiologists classically refer to these as "lower senses." Compared to the "higher senses" of vision and hearing, they are relatively primitive and yield much less detailed information concerning the stimuli that activate them. None the less, much of the research on the chemical senses has been moulded after the pattern of studies of vision and hearing. Witness the attempts of von Skramlik and others to derive taste-mixture equations in a manner analogous to those for color mixture.[1] The concern with such classic problems of sense function has resulted in a neglect of the other features that give the lower senses their special significance and importance for adjustive behavior. They merit study in their own right with particular regard to their role in preference and aversion behavior.

Such behavior appears to be relatively "stimulus bound." Thus the direct relevance of sensory stimulation for behavior is more obvious than in the case of the higher senses. This is not to say that the behavioral consequences of taste or olfactory stimulation are fixed and unchanging. The interaction of physiologic processes, environmental factors and learning can all be demonstrated. The classic work of Dr. Richter, our chairman, is a well known example. Other participants in this session will undoubtedly provide other examples.

The chemical senses and the behavior they control present a kind of model "stimulus-response" system of behavior, sometimes designated as "motivated behavior." Since all behavior is motivated, this designation implies that the motivational aspects here are more directly amenable to manipulation and direct observation. Thus, the study of the lower senses and the behavior they instigate is of significance for understanding behavior processes in general.

For want of time and because our laboratory has concentrated on the study of taste mechanisms, I shall restrict my discussion to that sense.† Our basic method, which has been described elsewhere,[2] is to record the afferent nerve impulses in the chorda tympani nerve of anesthetized animals. Rats, cats, rabbits and hamsters have been employed. Significant species differences have been found which appear to bear some relation to behavioral differences in the preference situation[2,3,4] However, for today's purposes we shall concentrate on the data from the rat and hamster.

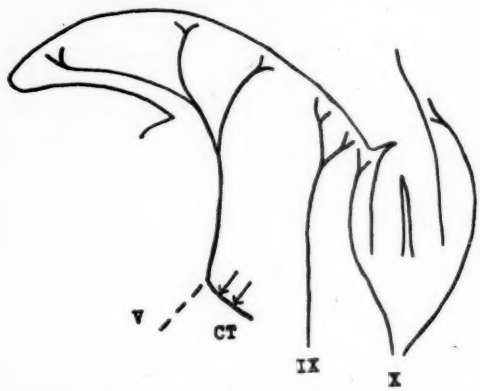

Fig. 1. Diagram of peripheral nerve supply to the tongue. V, trigeminal nerve; IX, glossopharyngeal n.; X, vagus n.; C. T., chorda tympani n. Arrows show the placement of recording electrodes.

* Professor, Department of Psychology, Brown University, Providence 12, R. I.

Presented at a Symposium on Nutrition and Behavior held at the Laboratory of Physiological Hygiene, University of Minnesota, April 27, 1956, with the cooperation of the National Vitamin Foundation, Inc., New York and under the sponsorship of the School of Public Health, University of Minnesota.

† Certain of the experiments reviewed herein were supported in part by a contract between the Office of Naval Research and Brown University.

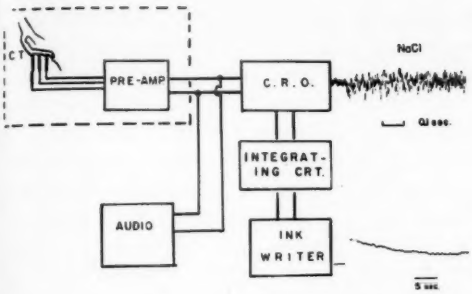

Fig. 2. Diagram of recording method. The two tracings on the right are sample records. C. R. O., cathode ray oscillograph.

METHODS

Figure 1 reviews the anatomic relations of the chorda tympani to the total nerve supply to the tongue. Most of the taste fibers leave the lingual nerve to pass centrally via the chorda tympani. The concentration of taste fibers here makes it especially suitable for electrophysiologic study. The method is illustrated in Figure 2 which shows the various features of the recording circuit. The usual amplifier oscillograph unit is supplemented by a summating or integrating circuit adjusted to give a running average of the impulse traffic up the nerve. The deflection of the summator recorder is proportional to both the frequency of discharge and number of fibers active. When the discharge drops to zero, the deflection of the summator likewise falls to zero. This circuit yields a quantitative measure of the typically asynchronous multifiber discha.ge.

When the activity in the chorda tympani nerve is so recorded, the application of quinine, hydrochloric acid, sodium chloride or sucrose solutions leads to a nerve response which first appears at some threshold concentration. The magnitude of the nerve response then increases approximately as a sigmoid function of the logarithm of the stimulus concentration. The response thus tends to level off or saturate at some high concentration value. The responses for the four typical taste stimuli enumerated above arrange themselves in the rat in the following order of thresholds from low to high: quinine, hydrochloric acid and sodium chloride at the same concentration, and sucrose, (lower graph of Figure 3). Note, however, that the magnitude of response in terms of voltage differs from substance to substance. Whereas NaCl and HCl yield substantial voltages and hence maximal deflections of the recorder, quinine and sucrose yield relatively small responses. This is one respect in which the species show significant differences. In the hamster, for example, sucrose, NaCl and HCl all yield large and approximately equal responses which, however, lie in different regions of the concentration scale. Only the quinine response is small. Differences of this sort among the species presumably reflect a difference in the number of nerve fibers mediating

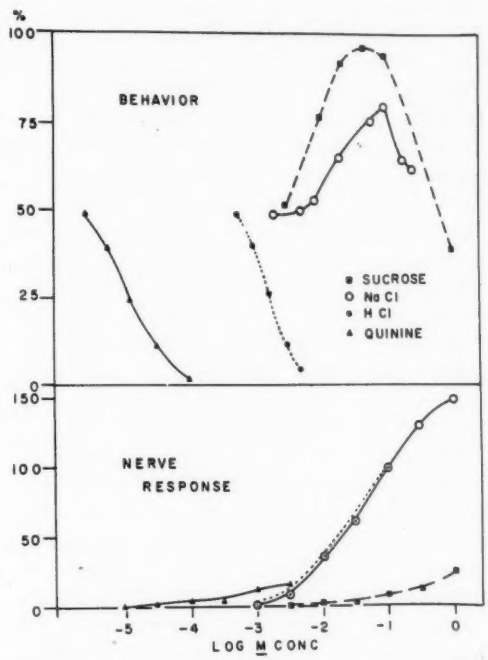

Fig. 3. Composite graph of behavioral and afferent neural responses. Upper figure shows preference-aversion responses. Lower figure shows neural responses (see text).

sensitivity to the different stimuli. A graph such as this summarizes the taste sensitivity in the average animal. The responses from animal to animal are remarkably constant.

THE PREFERENCE SITUATION

The upper part of Figure 3 represents responses by the intact normally behaving animal toward these same taste stimuli when presented in the typical two-bottle preference situation. This provides the animal with a a choice of two calibrated containers, one of which contains water, the other taste solution. In the case of preferred substances, the animal will drink mostly from the container with that substance. If the solution is avoided he will drink mostly from the water container. When different concentrations of the same solution are presented in an ascending order, it is possible to determine a preference or aversion threshold value. Aversion threshold may be defined as that concentration where the animal first begins to take more water and less solution. The response to solutions above this value (suprathreshold solutions) bears a systematic relation to concentration. This is conveniently measured by the volumes of water and taste solution ingested during a 24-hour *ad libitum* period. A percentage preference (or aversion) may be computed by dividing the volume of taste solution ingested by the total fluid ingested (i.e., water plus taste solution). Where the animal takes equal amounts of water and solution, the percentage equals 50 per cent. Values below 50 per cent indicate aversion, those above a preference. The upper part of Figure 3 shows that two substances, quinine and hydrochloride acid, are avoided and that the percentage aversion increases systematically with increase in concentration up to a complete avoidance. Two substances, sodium chloride and sucrose, are preferred. They both show the typical preference aversion function in which the intake or preference first rises to a maximum value and then falls off. With higher concentrations, these response curves will fall below the 50 per cent point when the stronger concentrations are avoided.

These curves show that the concentration ranges of the four stimuli correspond roughly on both the physiologic and behavioral response scales. The behavioral values shown are averages. The quinine hydrochloride values on 113 animals were compiled by Dr. R. M. Benjamin in our laboratory.[5] There is evidence of a definite behavioral response to concentrations at least one log unit below the point where the neural response is just detectable. The neural response threshold, of course, is limited by the "noise" level of the preparation, especially where the response magnitude is small. In addition, it must be remembered that our neural records sample only activity in the chorda tympani nerve. Until the contribution of the IXth nerve has been examined, our information on the total sensory input from the taste field will be incomplete. This qualification, of course, applies to all attempted correlations between behavior and chorda tympani records.

The response to HCl, obtained in a smaller group of 27 animals, is shown in the dotted curve. Here the neural response is substantial, beginning at around -3 (log M conc.). In both quinine and acid, the suprathreshold neural activity is related to strong and almost complete avoidance.

Sodium chloride is of interest because there is a clear and definite neural discharge very similar to that for acid. The behavior here indicates a preference rather than aversion. The afferent message, therefore, must contain information beyond mere *magnitude* of discharge which permits differential response. We have studied this problem by means of recordings from the single elements in the chorda tympani. These results have been reported elsewhere[2] and are not germaine to the present discussion. Note here that the electrophysiologic response appears and reaches a significant value before the preference becomes evident. This is contrary to the relation seen for the two aversive stimuli. Furthermore, we note a systematic rise to a maximum with a falling off in the range where the neural response is steadily rising.

Consider now the response to sugar. Here the neural response is small and the behavioral effect is a strong preference with the typical rising, maximal and falling phases. There is approximate agreement in the concentration range where the two effects occur. It should be noted that all data presented here reflect the behavior and physiologic response of nor-

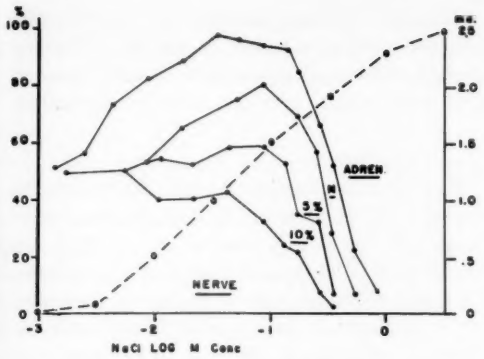

Fig. 4. Composite graph of neural response (broken line) and preference-aversion curves (solid lines) to sodium chloride solutions. Preference ordinate to the left, neural response ordinate to the right.

mal Wistar descendant rats maintained on an *ad libitum* diet.

That these relations are not fortuitous is indicated by the effect of denervating the tongue. Although the interference with taste sensitivity is not as great as originally believed[6] there is clear evidence of impairment in preference behavior following bilateral chorda tympani and IXth nerve removal.[7] Taste stimulation thus appears to be an initial sensory instigator of such behavior. Post-ingestion effects may modulate the behavior further.[8,9]

SODIUM CHLORIDE

Figure 4 shows an expanded scale for the NaCl response only. The neural response to NaCl (open circles, broken line) is similar to that shown in Figure 3. Four sets of data from preference studies carried out at various times in our laboratory are shown by the solid lines and dots. Each point is an average value. Curve N (normal) shows the full extent of the preference-aversion function with a peak preference at about 0.1 M (log −1). The 5 per cent and 10 per cent curves show the preference-aversion functions for two groups, one in which the diet was supplemented and mixed with additional NaCl to make a total salt content of 5 per cent. The lower curve shows the same data for the animal fed on a diet containing 10 per cent NaCl. Note the systematic shift in the preference curve as a function of the added salt. These figures do not show changes in the absolute volumes of fluid ingested, for under these conditions the fluid intake is much increased. The point here is that the relative intake of salt and water are shifted systematically from the normal, especially if we pay attention to the suprathreshold portions of the curve.

The top curve is the preference response shown by a group of adrenalectomized animals. Note that the entire preference-aversion function of the normal animal is enhanced. The salt-needy animal not only takes relatively more of the stronger solutions, he does so at all concentrations so that his preferential response becomes apparent at a lower concentration level. This observation, of course, is merely a repetition in our laboratory of Richter's classic experiments on salt need and self selection. The additional point here, however, is that the behavior toward the stimulus might be described as an exaggeration of that seen in the normal non-deprived animal.[10–13]

Young[14] speaks of two factors underlying the intake of NaCl solutions, (a) the properties of the stimulus (e.g. concentration of the solution) and (b) intra-organic factors (e.g. need produced by deprivation, etc.). We might say that the behavior is "stimulus bound" but modulated by variations in physiologic state.

THE NEURAL RESPONSE CURVE

So far I have said little about the neural response curve. The graph reproduces the points obtained from a number of normal animals. It was not obtained under any of the experimental conditions outlined. The only exception to this is for the threshold point which Dr. Bare and I reported on a number of years ago.[15] We found that the electrophysiologic thresholds for adrenalectomized and normal animals were essentially the same. We could find no evidence of an enhancement of sensitivity of the receptor as a result of adrenal insufficiency, which leads to such dramatic increases in the intake of salt solution. We have not determined the suprathreshold neural response under adrenalectomy. However, the confirmation of our finding of no difference in

sensitivity between normal and adrenalectomized animals by several workers utilizing the conditioned reflex method[16,17] appears to establish the fact that the receptor sensitivity curve is a relatively stable function. It is our belief that the function outlined by the broken line defines the basic operating limits of the taste receptor mechanism for the rat. Further, this appears to be a stable property of the receptor and is not influenced by changes in physiologic state of the internal environment bathing the taste cells.

From the form of the behavioral and neural response curves it appears that the normal animal can taste the salt solution, but is not motivated to ingest it. This is the only case where the neural response appears at a point lower on the concentration scale than does the preference effect. Both our data and that of Richter show the preference response to begin at a concentration value of around −2 on our scale. The preference behavior in the adrenalectomized animal is variously reported to appear from −2.5 to −3.2, which is in the range where the neural response first becomes obvious. Although Young and Chaplin[18] found no enhancement of preference behavior in adrenalectomy, Young[14] reported preference thresholds and/or evidence for discrimination of NaCl solutions by normal animals in the range −3 to −2.5. Only the data obtained by Harriman and MacLeod[17] by a conditioned shock avoidance method show discrimination of salt solutions at values far below these concentrations. They report values as low as −5 on our scale. This is lower than that obtained by Carr[16] using a similar method. Harriman and MacLeod took special precautions to lower the concentrations by small steps and to subject the animal to prolonged training. Discrepancies of nearly this magnitude between neural and behavior responses were noted above in our data in the case of quinine where the nerve responses were especially limited by the signal to noise ratio. The NaCl thresholds of single nerve fiber preparations which do not suffer from this limitation were found to lie at or above the −3 level.* Fibers sensitive to lower concentrations must be very few in number. Further work in the threshold range by both behavioral and physiologic methods seems warranted.

* This value is lower by approximately 1/4 of a log step than that first reported by Pfaffmann and Bare.[15]

SUGAR

We have one further recent observation to report, this time utilizing the sensitivity to sucrose.[19] As is well known, again from the work of Dr. Richter and others, the preference for sugar solutions can be markedly increased by a number of procedures, hunger and injection of insulin being two well known examples. It has been reported that human sensory thresholds were altered during hypoglycemia.[20] There is evidence that the taste receptors for sugar might be stimulated by a different kind of chemical mechanism than are the salt receptors. Thus, it seemed desirable to test the generality of our conclusion that the taste sensitivity at the periphery is unchanged by changes in the constituents of blood stream (short of excessive changes which might produce a generalized impairment).

As noted above, the hamster is one species in which there is a strong and readily observed response to sugar. Mr. Hagstrom and I examined the response in the chorda tympani of the hamster after the blood sugar was severely lowered by the injection of insulin. As a preliminary test to insure that differential suppression of the sugar receptors could occur, we determined the effect of the local action of Gymnemic acid, a drug which differentially suppresses sweet sensitivity in man, yet leaves salt sensitivity unimpaired. A 10-minute application of Gymnemic acid to the tongue surface reduced the response to sugar but had no effect on that to salt. We then recorded for a much longer period before and after the intraperitoneal administration of insulin. Blood sugar determinations were carried out after the administration of insulin, to insure its effectiveness. Five units of insulin were injected intraperitoneally. Prior to administration blood sugar values ranged from 40 to 70 mg/per 100 ml. After administration the values ranged from 7 to 23 mg/per 100 ml. No evidence was found of a differential enhancement or suppression of sensitivity to

sugar compared with that to NaCl. Lowering the blood sugar did not appear to affect sensitivity of the peripheral gustatory receptors.

SUMMARY

We have presented certain electrophysiologic observations on taste sensitivity and the correlation with behavioral responses to the same stimuli. An approximate agreement between the concentration ranges for the two responses was noted for the mean response curves, especially for suprathreshold effects.

Receptor function was studied under conditions that modify the physiologic state of the organism and with which pronounced changes in preference behavior have been reported. Under these circumstances no change in the gustatory response was noted. It is concluded that changes in behavior under these conditions reflect not a change in the peripheral afferent neural message but changes in its significance for central neural processes.

REFERENCES

1. VON SKRAMLIK.: *Handbuch der Physiologie der niederen Sinne.* Bd. 1, Thieme, Leipzig, 1925, pp. 454–462.
2. PFAFFMANN, C.: Gustatory nerve impulses in rat, cat, and rabbit. *J. Neurophysiol.* 18: 429, 1955.
3. BEIDLER, L. M., FISHMAN, I. Y., and HARDIMAN, C. W.: Species differences in taste responses. *Am. J. Physiol.* 181: 235, 1955.
4. CARPENTER, J. A.: Species differences in taste preferences. *J. Comp. & Physiol. Psychol.* 49: 139, 1956.
5. BENJAMIN, R. M.: *Cerebral mechanisms in gustatory discrimination.* Ph.D. Thesis, Brown University 1951.
6. RICHTER, C. P.: Transmission of taste sensation in animals. *Tr. Am. Neurol. A.* 65: 49, 1939.
7. PFAFFMANN, C.: Taste preference and aversion following lingual denervation. *J. Comp. & Physiol. Psychol.* 45: 393, 1952.
8. STELLAR, E., HYMAN, R., and SAMET, S.: Gastric factors controlling water and salt solution drinking. *J. Comp. & Physiol. Psychol.* 47: 47, 1954.
9. LE MAGNEN, J.: Immediate regulation of spontaneous intake of water and salt in the white rat in imposed states of hydromineral imbalance. *Compt. rend. Soc. Biol.* 147.1: 619, 1953.
10. BARE, J. K.: The specific hunger for sodium chloride in normal and adrenalectomized white rats. *J. Comp. & Physiol. Psychol.*, 42: 242, 1949.
11. RICHTER, C. P.: Increased salt appetite in adrenalectomized rats. *Am. J. Physiol.* 115: 155, 1936.
12. RICHTER, C. P.: Salt taste thresholds of normal and adrenalectomized rats. *Endocrinology* 24: 367, 1939.
13. RICHTER, C. P.: Self-regulatory functions. *Harvey Lecture* 38: 63, 1942.
14. YOUNG, P. T.: Palatability versus appetite as determinants of the critical concentrations of sucrose and sodium chloride. *Comp. Psychol. Monog.* 19: 1, 1949.
15. PFAFFMANN, C., and BARE, J. K.: Gustatory nerve discharges in normal and adrenalectomized rats. *J. Comp. & Physiol. Psychol.* 43: 320, 1950.
16. CARR, W. J.: The effect of adrenalectomy upon the NaCl taste threshold in rat. *J. Comp. & Physiol. Psychol.* 45: 377, 1952.
17. HARRIMAN, A. E., and MACLEOD, R. B.: Discriminative thresholds of salt for normal and adrenalectomized rats. *Am. J. Psychol.* 66: 465, 1953.
18. YOUNG, P. T., and CHAPLIN, J. P.: Preferences of adrenalectomized rats for salt solutions of different concentrations. *Comp. Psychol. Monog.* 19: 44, 1949.
19. PFAFFMANN, C., and HAGSTROM, E. C.: Factors influencing taste sensitivity to sugar. *Am. J. Physiol.*, 183: 651, 1955.
20. MAYER-GROSS, W., and WALKER, J. W.: Taste and taste selection of food in hypoglycemia. *Brit. J. Exp. Path.* 27: 297, 1946.

The Regulation of Food Intake

SOME EXPERIMENTS RELATING BEHAVIORAL, METABOLIC AND MORPHOLOGIC ASPECTS

By JAMES ANLIKER, PH.D.* AND JEAN MAYER, PH.D., D.SC.†

THE experiments reported in this paper are all concerned with the analysis of factors participating in the regulation of food intake in animals. The material may be divided into four categories as follows: (1) Relations between the hypothalamic structures and feeding-fasting behavior; (2) The nature of the physiologic stimulus to the hypothalamic satiety mechanism; (3) Some correlations between feeding-fasting behavior, blood glucose, and liver glycogen, and (4) The relationship between blood glucose and operant conditioning.

BEHAVIORAL METHOD

An effective technic for measuring and recording food intake is an obvious prerequisite for the analysis of its regulatory mechanisms. Considering the fact that food intake is normally accomplished through overt behavior on the part of an organism, we have applied a behavioral method to the problem of its measurement. The adaptation of operant conditioning apparatus and methods[1–3] to the measurement of food intake in the mouse is reported in detail elsewhere.[4] Briefly, the procedure is as follows: By placing a sensitive lever in a mouse's cage, we may observe that the mouse operates this device with an appreciable frequency in the absence of a history of food reward in this situation. This initial rate of responding is known as the *free operant level.* When lever-pressing responses are rewarded with food, their frequency tends to increase (provided, of course, that the mouse has been deprived of food for some time). If each lever-press produces a pellet of food, the mouse soon becomes satiated and ceases to press the lever at a rate that is higher than the free operant level. However, since no food is available unless the lever is pressed, and since it is impossible for the mouse to hoard an appreciable quantity of food because of the design of the cage, periods of nonresponding are also periods of noneating. As deprivation increases, the probability of responding increases. Ultimately, the mouse presses the lever and eats, and so forth. In this way periods of feeding alternate with periods of abstaining from food. Under relatively constant environmental conditions (including stability and uniformity of the diet), the mouse develops a fairly consistent pattern of feeding and fasting. Through the use of a suitable recording device an accurate account of the number of pellets delivered, as well as the time of delivery of each, can be obtained. It is possible to insure a close correlation between pellet-delivery and pellet-consumption by rewarding only a fixed ratio of the responses (e.g., by delivering one pellet after 25 responses).

From the Department of Nutrition, School of Public Health, Harvard University, Boston, Mass.

* Research Associate, Department of Nutrition, School of Public Health, Harvard University, Boston, Mass.

† Assistant Professor, Department of Nutrition, School of Public Health, Harvard University, Boston, Mass.

Supported in part by Grant No. A-49, National Institute of Arthritis and Metabolism, National Institutes of Health, Bethesda, Maryland; Sugar Research Foundation, New York; Kellogg Company, Battle Creek, Michigan; and The Nutrition Foundation, Inc., New York.

Presented at a Symposium on Nutrition and Behavior held at the Laboratory of Physiological Hygiene, University of Minnesota, April 27, 1956, with the cooperation of the National Vitamin Foundation, Inc., New York and under the sponsorship of the School of Public Health, University of Minnesota.

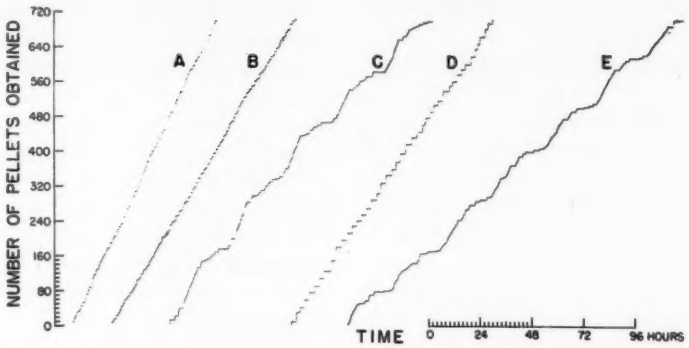

Fig. 1. Cumulative records of pellets obtained by mice on a schedule of reward that allows one pellet of food (approximately 0.04 g) for every 25 operations of the lever. Records A, B, and C are from Swiss mice: (A) goldthioglucose obese, (B) hypothalamic obese, and (C) normal. Records D and E are from mice of a Bar Harbor stock that produces mice exhibiting the hereditary obese-hyperglycemic syndrome (D) and normal littermate (E). Observe that the 24-hour cyclical changes in rate of feeding evidenced in the records of normal mice (C, E) are either absent or barely discernible in the records of hyperphagic mice (A, B, D).

THE RELATIONSHIP BETWEEN THE HYPOTHALAMUS AND FEEDING BEHAVIOR

It is now well-established that lesions in the ventromedial hypothalamus result in hyperphagia.[5,6] Lesions in the lateral hypothalamus, on the other hand, produce hypophagia or aphagia.[7,8] Recently, it has been demonstrated that the hyperphagia induced by goldthioglucose treatment is also attributable to destruction in the ventromedial hypothalamus.[9] Figure 1 shows the feeding patterns for a hypothalamic hyperphagic mouse in which the lesions were produced by goldthioglucose treatment (A) a hypothalamic hyperphagic mouse in which the lesions were produced by electrocoagulation (B), and a normal mouse (C). It is readily apparent that the diurnal changes in rate of feeding are greatly reduced or barely perceptible in both types of hypothalamic hyperphagia.

These results may be interpreted as supporting the hypothesis that the ventromedial area acts to inhibit feeding behavior and that in its absence hyperphagia results. It seems improbable that the ventromedial hypothalamus contains the only mechanism for the inhibition of feeding behavior because even in animals exhibiting extreme hyperphagia, there is a periodic cessation of eating. However, we should not overlook the infrequent but recurrent instances in which rats with hypothalamic lesions die from overeating. Before turning their entire attention to other inhibitory mechanisms; such as, pain resulting from gastric distention, etc., investigators will do well to determine the amount of residual inhibitory capacity attributable to undestroyed ventromedial cells since lesions are seldom, if ever, complete. The fact that 24-hour cycles tend to become increasingly prominent as the animal approaches the static phase of obesity might be interpreted as evidence for the reassertion of inhibitory control by remaining ventromedial tissue under more favorable metabolic conditions (lipostatic hypothesis), or, possibly, because of partial recovery of injured, but not destroyed, neurons.

Teitelbaum and Campbell[11] have reported recently that hypothalamic hyperphagic rats fed a liquid diet, the consumption of which was recorded by a drinkometer, did not eat a larger number (8 to 12) of meals in a 24-hour period than did normal rats; the hyperphagic rats ate more during each meal. This suggests that, in rats at least, the ventromedial hypothalamus normally participates in the termination of individual meals.

PHYSIOLOGIC STIMULUS TO THE HYPOTHALAMIC SATIETY CENTER

Evidence favoring a glucoreceptive intermediary between metabolic processes and central neural regulatory mechanisms has been reviewed elsewhere.[10,12] One of the most cogent arguments in favor of the glucoreceptor theory is furnished by the evidence that the chemical compound, goldthioglucose, induces hyperphagia in mice.

It has been shown[9] that the hypothalami of goldthioglucose-injected mice show definite lesions within one to three days, involving edema, pyknosis, and degeneration of nerve cells in the ventromedial area of the hypothalamus. Larsson[13] found that in fasted rats this area concentrates radioglucose and radiophosphate as compared with a control area from another part of the hypothalamus.

It is well-known that the heavy metals are extremely toxic to cells. Consequently, we are inclined to the view that, because the ventromedial area contains cells that concentrate glucose and because the gold is linked to the glucose, these cells are selectively poisoned. That is, they manage to concentrate a toxic dose of gold. This hypothesis is supported by the evidence[14] that a great variety of other goldthiocompounds do not cause hypothalamic damage or induce hyperphagia. For example, goldthiomalate, a compound of equivalent toxicity, does not induce hyperphagia and does not produce demonstrable hypothalamic damage.[15]

Likewise, goldthiosorbitol (a compound extremely similar in structure to goldthioglucose), goldthioglycerol and goldthiocaproic acid, (two compounds in which the gold is tied by a sulphur bridge to substances normally involved in fat metabolism) do not produce lesions or induce hyperphagia.[16] Furthermore, it was shown in the rat that on administration of the same dose of goldthioglucose (1 mg/gm of body weight, the LD_{50} for mice) produces cell degeneration in the same ventromedial area as in the mouse but the gold is so generally toxic to the rat that it does not survive to show the hyperphagia. It has been reported that feeding the animals before injection of goldthioglucose diminishes the incidence of permanent damage and hyperphagia by 30 to 50 per cent.[13]

Thus, gold appears to concentrate in toxic amounts in the ventromedial areas when it is linked to glucose and not when it is linked to other substances or metabolites. Glucose and other compounds containing glucose are apparently concentrated in the ventromedial area as readily as goldthioglucose and hence reduce the rate of accumulation of the latter compound in these cells. We believe that these data provide relatively strong support for the view that there are glucoreceptors in the ventromedial hypothalamus.

OBESE HYPERGLYCEMIC SYNDROME IN MICE

In Figure 1 curves D and E are representative of the hyperphagic mouse bearing the *ob ob* gene and its normophagic litter mate, respectively. The fact that the hereditarily obese mouse has an apparently intact ventromedial hypothalamus and is hyperphagic even while hyperglycemic might appear to contradict the glucostatic theory. However, it is possible to place these findings in harmony with the theory if we consider the fact that this organism exhibits abnormalities of carbohydrate metabolism (including a sixfold acceleration in rate of turnover of liver glycogen) and that it is quite possible that the receptor area is simply less responsive to blood glucose.

RELATIONSHIP BETWEEN FEEDING BEHAVIOR AND LIVER GLYCOGEN

Figure 2 permits comparison of the diurnal pattern of feeding behavior and diurnal variation in liver glycogen. In this study liver glycogen was determined by sacrificing six mice every other hour around the clock starting at 1:00 p.m. The amount of liver glycogen was determined* according to the method described by Good, Kramer, and Somogyi.[17] The feeding patterns were obtained from six thoroughly-trained normal mice, the record being that of the fifth consecutive day in the Skinner box. From these data it is apparent that the feeding pattern of normal mice is characterized by a high rate of feeding in the afternoon and evening and a tapering off of the feeding rate during the night to a very low rate of feeding in the

* We are indebted to Dr. Konosuke Tomabechi for these measurements.

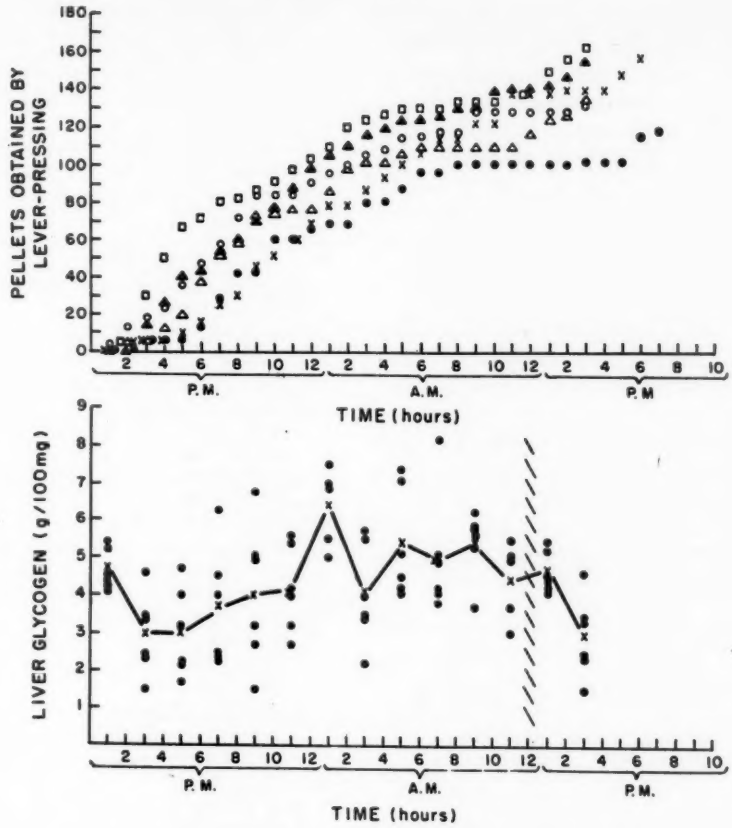

Fig. 2. Comparison of diurnal variations in feeding behavior and in amount of liver glycogen in normal mice. Upper portion of figure contains cumulative records, for six normal mice, of pellets obtained by lever-pressing. The lower portion of the figure shows the quantities of liver glycogen found in groups of mice sacrificed at 2-hour intervals around the clock, starting at 1 p.m. The data located to the right of the diagonal bars are simply duplicates of the data for the first two groups; this arrangement is intended to facilitate comparison between the upper and lower graphs.

morning. Liver glycogen accordingly is lowest at the time the mice begin their rapid feeding phase, rises along with rapid feeding, levels off during the night and starts falling in the early morning hours. From these data we tentatively conclude that there is a rate of feeding above which liver glycogen accumulates and below which liver glycogen is dissipated. Liver glycogen represents the most readily available source of glucose reserves. It is well known that food deprivation leads to a depletion of glycogen and that satiation is associated with a rise in blood sugar which is counteracted by insulin secretion and the formation of liver glycogen. Considering the fact that the pancreatic hormone, glucagon has the capacity to increase the amount of active phosphorylase in the liver,[18] one might suppose that this hormone is at least partially responsible for the glycogenolysis associated with fasting. However, the physiologic conditions in which glucagon is released from the pancreas are not currently known. Myers et al.[19] have demonstrated that glucagon produces a prompt rise in the blood sugar of the hepatic vein. Recent unpublished experiments performed in our laboratory have shown that sub-

cutaneous injections of glucagon in sufficiently large amounts will produce a transient inhibition of feeding activities of mice commencing about 15 to 20 minutes after injection and lasting for a variable number of minutes depending upon the amount injected. Glucagon has also been shown to inhibit gastric contractions in man[24] and in rats.[21] There is good evidence that parenteral injections of insulin in moderate dosages produces an increase in the rate of eating in animals[22] and in men.[23]

Taken together, these observations confirm the generally accepted view that blood glucose and liver glycogen usually rise after feeding and then begin to fall sometime after feeding has ceased and that feeding and fasting behavior correspond in a general way to the rise and fall of blood glucose and liver glycogen.

RELATIONSHIP BETWEEN BLOOD GLUCOSE AND BEHAVIORAL CONDITIONING (LEARNING)

Coppock and Chambers[24] have demonstrated that in the rat intravenous glucose has a reinforcing effect; that is to say, it is possible to condition responses by providing intravenous glucose as a "reward." This experiment suggests to us a whole series of studies of the capacity of different organisms to discriminate intravenous substances under various conditions.

SUMMARY

Experimental evidence was presented which supports the view that the hypothalamus contains a "feeding" center and a "satiety" center. The satiety center obtains its information from the bloodstream via glucoreceptors. Destruction of the satiety center acts to release the feeding center from the inhibitory influence of the satiety center and this results in hyperphagia. Changes in blood glucose and liver glycogen resulting from feeding and fasting and from parenteral injections of glucagon and insulin are likewise in conformity with the glucostatic theory of the regulation of food intake. Finally, the fact that intravenous glucose is effective as a reward in operant conditioning indicates that rats, and presumably other animals, are capable of discriminating changes in blood glucose.

REFERENCES

1. Skinner, B. F.: The Behavior of Organisms. D. Appleton-Century, New York, 1938.
2. Skinner, B. F.: The experimental analysis of behavior. *Proc. and Papers, 13th Int. Cong. Psychol.* Stockholm, 1951.
3. Ferster, C. B.: The use of the free operant in the analysis of behavior. *Psychol. Bull.* 50: 263, 1953.
4. Anliker, J., and Mayer, J.: An operant conditioning technique for studying feeding-fasting patterns in normal and obese mice. *J. Applied Physiol.* 8: 667, 1956.
5. Brobeck, J. R.: Mechanism of the development of obesity in animals with hypothalamic lesions. *Physiol. Rev.* 26: 541, 1946.
6. Mayer, J.: Genetic, traumatic and environmental factors in the etiology of obesity. Physiol. Rev. 33: 472, 1953.
7. Anand, B. K., and Brobeck, J. R.: Localization of "feeding center" in hypothalamus of rat. *Proc. Soc. Exp. Biol. & Med.* 77: 323, 1951.
8. Teitelbaum, P., and Stellar, E.: Recovery from the failure to eat produced by hypothalamic lesions. *Science*, 120: 894, 1954.
9. Marshall, N. B., Barrnett, R. J., and Mayer, J.: Hypothalamic lesions in goldthioglucose in mice. *Proc. Soc. Exp. Biol. & Med.* 90: 240, 1955.
10. Mayer, J.: Regulation of energy intake and the body weight: The glucostatic theory and the lipostatic hypothesis. *Ann. New York Acad. Sc.* 63: 15, 1955.
11. Teitelbaum, P., and Campbell, B. A.: Patterns of food ingestion in hyperphagic and normal rats. Am. Psychol. 11: 491, 1956.
12. Mayer, J.: *La régulation de l'appétit, Proc. XXth Int. Physiol. Cong.* Brussels, 1956.
13. Forssberg, A., and Larson, S.: On the hypothalamic organization of the nervous mechanism regulating food intake. II. Studies of isotope and chemical composition in the hypothalamic region of hungry and fed rats. *Acta Physiol. Scand.* 32: suppl. 115, part 2: 40, 1954.
14. Mayer, J., and Marshall, N. B.: Mode d'action de l'aurothioglucose et régulation glucostatique de la nutrition. *Compt. rend. Acad. de Sc.*, 242: 169, 1956.
15. Marshall, N. B., and Mayer, J.: Energy balance in goldthioglucose obesity. *Am. J. Physiol.* 178: 271, 1954.
16. Mayer, J., and Marshall, N. B.: To be published.
17. Good, C. A., Kramer, H., and Somogyi, M.: The determination of glycogen. *J. Biol. Chem.* 100: 485, 1933.
18. Sutherland, E. W., and Cori, C. F.: Influence of insulin preparations on glycogenolysis in liver slices. *J. Biol. Chem.* 172: 737, 1948.

19. MYERS, J. D., KIBLER, R. F., and TAYLOR, W J.: Effects of pancreatic hyperglycemic factor on hepatic carbohydrate metabolism in man. *Fed. Proc.* 11: 111, 1952.
20. STUNKARD, A. J., VAN ITALLIE, T. B., and REISS, B. B. The mechanism of satiety: effect of glucagon on gastric hunger contractions in man. *Proc. Soc. Exper. Biol. & Med.* 89: 258, 1955.
21. VAN ITALLIE, T. B. Personal communication, 1956.
22. MORGAN, C. T., and MORGAN, J. D.: Studies in hunger: I. The effects of insulin upon the rat's rate of eating. *J. Genet. Psychol.* 67: 153, 1940.
23. FREYBURG, R. H. A study of the value of insulin in undernutrition. *Am. J. M. Sc.*, 190: 28, 1935.
24. COPPOCK, H. W., and CHAMBERS, R. M.: Reinforcement of positionp reference by automatic intravenous injections of glucose. *J. Comp. Physiol. Psychol.* 47: 355, 1954.

Psychologic Factors Regulating the Feeding Process

By PAUL THOMAS YOUNG, PH.D.*

WORKERS in the fields of psychology, physiology, nutrition and related areas have frequently assumed that the quantity of food ingested per day by an animal is a measure of some hypothetic entity called "appetite." For example, in the pioneer studies of Richter the operational definition of appetite has been "intake per day." If the daily intake of a 3 per cent sodium chloride solution increases after adrenalectomy, it is said that the appetite for sodium chloride has increased. Again, if rats depleted of vitamin B stop eating carbohydrate and ingest large quantities of fat, it is said that the appetite for carbohydrate has decreased and that the appetite for fat has increased. Independent variability of intake is the main evidence for existence of separate appetites (or specific hungers) for protein, fat, carbohydrate, water, minerals and vitamins.

This assumption, that quantity of food consumed per day is a measure of "appetite," agrees with a common sense notion that the better one likes a food the more one eats of it. The cook is flattered when all the biscuits are eaten but disappointed if they remain on the plate untouched! Yet, the view that the quantity of food consumed measures a unitary "appetite" must be abandoned for the reason that intake does not depend upon a single factor.

There are at least four kinds of factors that regulate intake: (a) affective arousals determined by excitation of the head receptors and by post-ingestion conditions; (b) feeding habits and attitudes based upon dietary experience; (c) neural organizations that facilitate or inhibit ingestion of foods; and (d) the chemical constitution of the organism as determined by the genes and by dietary history.

I wish to consider several of these factors and their interrelations and for convenience will consider them under three main headings: (1) Taste and post-ingestion regulators of intake. (2) The relation between bodily needs and feeding habits. (3) The psychologic and chemical bases for the organization of feeding habits.

At the start, however, I should say a few words about the two main types of apparatus we have used in our experiments.[1,13] One type permits the rat to make a choice between two kinds of foodstuff (solids or fluids) that are presented simultaneously and briefly for choice. The other kind of apparatus records fluid intake continuously during brief exposure (5 to 20 minutes) or continuously for 24 hours or more.

TASTE AND POST-INGESTION REGULATORS OF INTAKE

McCleary[3] distinguished between taste factors and post-ingestion factors in the regulation of intake. He demonstrated the importance of the internal determinants by introducing solutions through a tube directly into the stomach of the rat. He found that pre-loading the stomach with glucose or fructose solutions depressed the ingestion of glucose after the tube had been removed. McCleary believes that osmotic pressure (varying with the kind of substance and the concentration) is the important factor associated with

* Professor of Psychology, University of Illinois, Urbana, Illinois.

Presented at a Symposium on Nutrition and Behavior held at the Laboratory of Physiological Hygiene, University of Minnesota, April 27, 1956, with the cooperation of the National Vitamin Foundation, Inc., New York and under the sponsorship of the School of Public Health, University of Minnesota.

depression of intake. He found that pre-loads of urea, sodium chloride and glucose, when matched for osmotic pressure, produced equivalent amounts of depression of ingestion. Interestingly enough, pre-loads of hypotonic saccharin solutions did not depress the subsequent ingestion of glucose solutions and McCleary suggests that the intake of saccharin solutions is regulated by taste factors as distinct from post-ingestion factors.

Shuford[4] studied the relation between the head receptors and the internal regulators with a different method but his results agree completely with those of McCleary. Shuford arbitrarily selected for study three concentrations of glucose solution, namely, 5, 15 and 35 per cent, by weight. For each of these glucose solutions he determined the concentration of a sucrose solution that was equally acceptable to his panel of 30 albino rats. In determining equally acceptable (isohedonic) concentrations a series of preference tests were run in which a constant concentration of glucose was compared, in turn, with several concentrations of sucrose solutions. From the results of preference tests the isohedonic values were computed.

Repeated tests have shown that when the subject has only a brief contact with a sugar solution or an immediate choice between two sugar solutions the *sweeter* is regularly preferred to the less sweet. With sucrose solutions, for example, both rats and men prefer the higher concentration to the lower all the way up the continuum from zero (distilled water) to a saturated solution.[2] The reason why this fact is important is that if one depends upon the volume of intake to determine relative acceptability, one finds an optimal concentration at about 8 or 9 per cent but no such optimum exists when the subject is limited to a brief contact with an immediate choice. The sweeter solution is regularly preferred to the less sweet.

In Shuford's tests each of the 30 rats was given a 20-minute drinking test with six solutions presented, one at a time. The six solutions were presented according to a counterbalanced Latin square design.

Figure 1 shows the cumulative mean intake of the solutions. These pairs of curves demonstrate the following points:

(1) During the first few minutes of drinking,

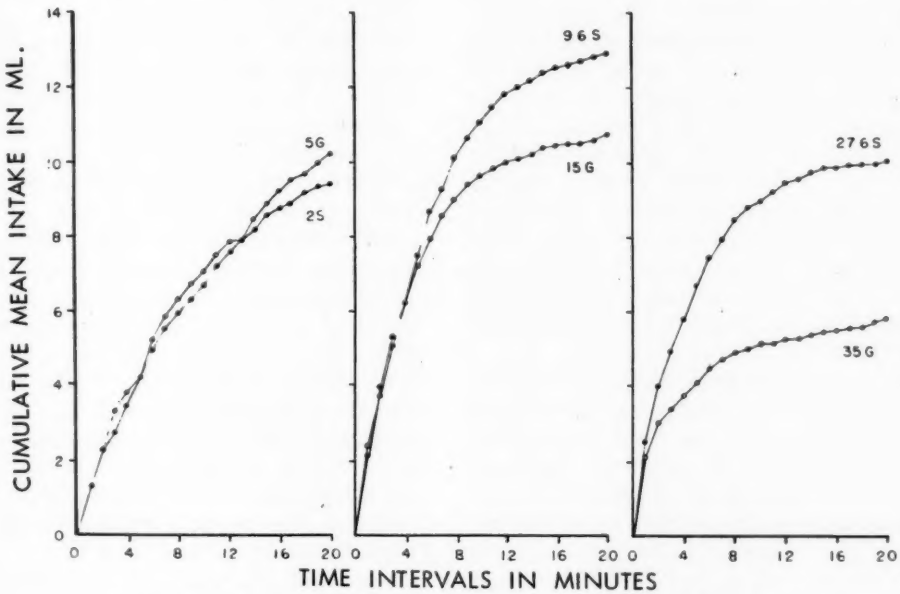

Fig. 1. Intake curves for isohedonic solutions of glucose (G) and sucrose (S).

the equally acceptable sugar solutions were consumed at the same rate.

(2) The initial rate of ingestion is a function of the concentration or degree of sweetness. This can be seen by comparing the initial slopes of the three pairs of curves. This initial rate of acceptance follows the rule that a higher concentration of sugar solution is more acceptable (as shown by the rate of acceptance) than a lower concentration.

(3) The inhibition of ingestion is definitely related to the osmotic pressure of the substance in solution. Osmotic pressures for the equally acceptable pairs of solutions are shown in Table I.

TABLE I

Concentrations (per cent by weight) of isohedonic solutions		Osmotic pressures (in atmospheres) corresponding to isohedonic concentrations	
Glucose	Sucrose	Glucose	Sucrose
5	2.0	7	1.4
15	9.6	23	8.0
35	27.6	74	30.0

If the curves for the 5 per cent glucose and 2 per cent sucrose solutions are compared, the similarity is remarkable. The taste factor evidently determines the shape of these curves since all rats were non-thirsty before and during the tests. The divergence of curves for the other isohedonic pairs of solutions can be attributed to the operation of a post-ingestion factor since the two kinds of sugar solution differ greatly in osmotic pressure but not in sweetness or palatability. The shape of the intake curves, then, is determined by two opposing factors: a facilitating taste factor and an inhibiting post-ingestion factor, related to osmotic pressure.

The work of McCleary and Shuford clearly demonstrates that intake is regulated by two distinct groups of factors: head receptor factors and internal organic processes. Hence we can not rely upon the total quantity of food ingested as a measure of some hypothetic entity called "appetite." The post-ingestion inhibition of intake is closely related to what we commonly call the satiation of appetite; but appetite, in this sense, is distinct from palatability.

THE RELATION BETWEEN BODILY NEEDS AND FEEDING HABITS

The early claim of J. M. Evvard that the appetite of the pig is a reliable indication of physiologic need found partial support in the self-selection feeding experiments of C. M. Davis with infants and children and in the numerous self-selection experiments of Curt Richter with rats, as well as in the work of W. F. Dove and various other investigators. In 1944, however, the Editors of *Nutrition Reviews*,[5] after considering available evidence, published the following six statements about appetites as a guide to nutrition:

(1) Appetites are often fickle and unpredictable.

(2) Appetites may be trivial in origin.

(3) Nutrition based upon appetites is not universally successful.

(4) Individual animals vary in their ability to make choices that will improve their nutritional status.

(5) Factors affecting human appetites may be expected to be more numerous and more complex than those affecting the appetites of animals.

(6) From the evidence, self-selection of diets appears to be inferior to scientific evaluation of diets for the maintenance of good nutrition.

In the light of this blast from the nutritionists, and even apart from it, no one today would have the temerity to claim that the food choices of animals are an infallible guide to correct nutrition. On the other hand, there is danger that these statements will lead to an opposite extreme view: that there is no relation at all between food selections and bodily needs. The truth lies somewhere between these extreme views. The experimentalist must ask questions like these: To what extent are the food selections of animals in agreement with their metabolic needs? What are the mechanisms that regulate the selection of foods and how are these mechanisms related to bodily needs?

A dramatic example of the relation between bodily need and feeding habit appeared

unexpectedly in one of our experiments.[6] Groups of rats were maintained upon a self-selected diet in large cafeteria cages. From time to time they were given brief-exposure preference tests between two of the components of their diet: sucrose and casein. A clear and consistent preference of sucrose to casein developed. Then the protein was removed from the diet, all other elements remaining the same. After 25 to 32 days of depletion there were objective signs of protein starvation: loss of weight, reduction of general food intake, development of peptic ulcers, etc. With severe protein starvation the rats continued to select sugar (which they did not need) in preference to casein (which they did need). This was a very unwise choice. Then we tested the rats with a new technic in which the test-foods were widely separated but located in familiar places. The animals had to choose between running to sugar or running to casein. Under the new testing conditions the rats quickly learned to run to casein. The preference was clear and consistent. At the close of the experiment it was possible to put the animals on the standard preference tester and demonstrate a preference of sugar to casein. Five minutes later the same rats, on another apparatus, clearly revealed the reverse preference, a preference of casein to sugar. The second choice was a wise one agreeing completely with manifest bodily needs.

The interpretation of this result, made after a series of control experiments, is as follows: The initial preference of sugar to casein was based upon palatability relations. It is commonly known that rats *like* sugar and *do not like* casein (although they will accept it). The first preferential habit (for sugar) was persistent. This habit stabilized food selections even when the choice was inappropriate. The introduction of a different technic for testing preferences required the animals to form a new habit and this new habit developed in agreement with manifest bodily needs. The general underlying principle is this: *New habits tend to form in agreement with bodily needs, but established habits tend to persist as regulators of food selection even when the food selections are out of line with bodily needs.* In other words, feeding habits once formed tend to stabilize the choice of foods independently of need but habits do tend to form in agreement with needs.

The question remains as to how a need for protein led to the organization of a protein-selecting habit. It is possible that the protein starvation changed the palatability of casein so that it tasted better to the rats, but it is also possible that some organic relief from the distress that was produced by severe protein starvation was the basis of the new habit. This is a problem that requires further study.

In a well-known investigation of Harris *et al.*[7] rats were depleted of thiamine. They were then given a choice between diets containing a small but sufficient quantity of thiamine and diets that lacked the vitamin. Under these conditions the animals failed to discriminate between adequate and inadequate diets. The vitamin-depleted rats were then educated. They were given *only* the adequate diet, marked by a particular flavor, for a few days. When they had associated relief from organic distress with a particular flavor they continued to select the diet with that flavor even after the vitamin had been withdrawn and placed in another diet. Apparently a diet must be labeled by a flavor and, further, it must be associated with relief from organic distress before the dietary habit will form.

Other work upon the organization of dietary habits has been reported. Scott and Quint[8] published observations upon the appetites for certain vitamins. They report that rats maintained upon an adequate diet do not show any appetite for thiamine, riboflavin, or pyridoxine. But if the animals are maintained upon a diet deficient in these vitamins, they develop an appetite for them. Animals depleted of pantothenate, however, do not develop an appetite for this vitamin unless it is placed in a food that is clearly labeled with a flavor; even then some of the rats fail to select the vitamin-containing diet.

Scott and Verney[9] believe that the appetites for thiamine, riboflavin, and pyridoxine are *learned*. These appetites are probably learned by vitamin-depleted rats through associating the eating of a vitamin-containing diet with

some beneficial experience that had occurred at the time of the ingestion of the adequate diet. Scott and Verney thus agree with the views expressed by Harris *et al.*[7]

In summary, it is clear that feeding habits may or may not agree with bodily needs, that such habits tend to stabilize the selection of foods quite apart from bodily needs and, most emphatically, that some food habits *are organized* in complete agreement with bodily needs.

THE PSYCHOLOGIC BASIS FOR THE ORGANIZATION OF FEEDING HABITS

It is important, in the light of the above evidence, to consider the basis of habit organization. Upon what do feeding habits depend? There are two kinds of answers that I should like to consider: The first is psychologic, the second is chemical.

In considering the hedonic basis for the organization of feeding habits it is necessary to distinguish between affective arousals that are dependent upon stimulation of the head receptors and affective arousals that are dependent upon internal organic conditions.

Palatability and Appetite

The term *palatability* refers to the hedonic value of a foodstuff that is dependent upon its taste, aroma, texture, temperature, appearance, etc., and that may be modified by its surroundings. In other words, palatability implies an affective arousal that is dependent upon excitations of the head receptors. The hedonic hypothesis states that animals learn to select and to seek foods which they *like* rather than foods which they *need*, or require nutritionally, but there is a considerable agreement between what an animal likes and what he needs. Similarly, animals avoid foods which they *dislike* rather than foods that are harmful but, again, animals tend to dislike foods that are injurious. The term *appetite*, as used in everyday life, implies a conscious desire for a specific kind of foodstuff. Appetites are built up through depletion of needed substances; they are satiated through ingestion of the needed substances.

The relation between palatability and appetite will be illustrated by a recent experiment[10] upon the acceptability of different kinds of drinking water. The subjects in the illustrative experiments were 12 adult female rats. To eliminate thirst an unlimited supply of tap water was kept continuously present in the cages where they lived. The rats were taken from these cages into an adjoining room where their responses to two kinds of drinking water were immediately tested by the brief-exposure preference method. Each animal was given a series of choices between tap water and distilled water. The animals were thoroughly familiar with both kinds of water prior to the tests and with the testing procedure.

Under these conditions 5 of the 12 animals selected tap water in preference to distilled water. The choice of tap water was statistically significant at better than the one per cent level of confidence. Animals that did not meet the criterion of statistical significance still took tap water more frequently than distilled. The group as a whole selected tap water in 67 per cent of all choices whereas a chance selection would yield 50 per cent.

After the preference for tap water had been clearly established the rats were made thirsty by depriving them of water for 20 to 23 hours prior to the preference tests. As expected, the thirsty rats were much more active upon the apparatus. Minute for minute, during the 12-minute tests, the thirsty rats made more runs than the non-thirsty. But the thirsty animals were much less discriminating. No thirsty rat showed a preference for tap water and only one animal revealed any preference at all (a temporary preference for distilled water).

How can we interpret this result? The initial choice of tap water, I assume, is based upon a palatability difference. Rats and men like the taste of tap water better than the taste of distilled water. In our rats thirst raised the level of acceptability of both kinds of water. The increment in acceptability attributed to thirst obscured the relatively small difference in palatability.

The experiment, I think, demonstrates an

important relation between palatability and thirst as separate but interrelated determinants of the acceptability of different kinds of drinking water.

Affective Arousals with an Internal Organic Basis

It should be pointed out that affective arousal occurs *after* foods have been ingested. A square meal, to a healthy person, brings a feeling of comfort and well-being; and the ingestion of certain foods, e.g., green apples, produces acute gastric distress.

We know that the deprivation of oxygen or water or the accustomed maintenance food quickly produces acute distress. Further, as we know, a diet that lacks an essential element such as protein or thiamine sooner or later produces a specific deficiency. Distress produced through depletion does not necessarily imply any craving, or appetite, to remove it. The organism may suffer from a dietary deficiency and have no knowledge of the nature and cause of his distress. But if *relief* from discomfort can be associated with the ingestion of a particular kind of food, then the organism can learn the behavior necessary to accept and pursue a particular kind of food.

Accordingly, feelings of comfort and discomfort, based upon the eating of certain foods and also upon depletion or repletion, are clearly affective arousals. In a psychologic sense, they are affective arousals just as truly as the pleasantness from a sweet taste or the unpleasantness from a bitter taste.

In general, it is our hypothesis that feeding habits are organized on the basis of affective arousals. These arousals may be based upon the taste, smell, temperature and texture of foods, i.e., upon palatability. Or affective arousals may be associated with the after-effects of eating or of being deprived of nutritive substances. Thus the affective-arousal hypothesis extends far beyond palatability effects to take account of affective arousals produced by post ingestion conditions and through depletions of dietary substances.

CHEMICAL REGULATORS OF FOOD PREFERENCES AND ADDICTIONS

Food Preferences and Body Chemistry

Our studies with rats have shown that food preferences are learned. When given an opportunity to choose between two foods, rats learn to select one in preference to another. The increasing frequency of choice we have called a *preferential trend*. The preferential trend indicates that the subject is learning to discriminate preferentially between two test-foods. Preferences develop quickly or slowly. When a preference develops quickly we assume that the foods are widely separated in acceptability; when the trend moves slowly we assume that the foods are near together in acceptability. In special instances where no preference develops we assume an equality or near equality in the level of acceptability of the test-foods.

We have repeatedly found that when all the rats in a group are maintained upon a constant diet the animals in the group tend to develop one and the same pattern of food preferences. There are occasional signs of individuality in preference. For example, in one study[11] 42 rats were given a preference test between casein and sucrose. Of these, 41 preferred sucrose and one consistently preferred casein. Why this animal differed from the rest of the group we do not know, but from time to time such individual differences have been observed. Possibly individual differences in food selection depend upon individual differences in body chemistry.

We have demonstrated that the pattern of preferences revealed by the group is dependent upon the diet. For example, if rats are fed a protein-deficient diet, the preferential rating of casein is higher than that of surcrose but with a protein-adequate diet, casein has a low rating.

My guess is that food preferences and body chemistry are very significantly related to each other. There are doubtless species' differences in food preferences that depend upon differences in the chemical constitution of organisms, but very little is known about this matter. There is great need for research in

which biochemical controls are combined with precise studies of preferential patterns.

Addictions and Body Chemistry

Hebb[12] distinguishes between habits and addictions. Both feeding habits and addictions are learned and both have a neural basis; but the addiction, as distinct from the habit, has a biochemical basis.

Hebb pointed out that an objective science of behavior must deal with specific patterns of food-seeking behavior that are learned, or acquired. Hence the problem of specific hunger is really a problem of how specific food-seeking patterns are acquired. Addictions, such as the addiction to alcohol or morphine, are acquired gradually; they take weeks or months to develop. When an addiction has once developed there is some kind of internal chemical adaptation that makes it necessary for the organism to maintain a blood concentration of a specific substance for the maintenance of stable neural functioning. When the addiction has become established the addict is in discomfort and often in emotional distress if he is deprived of the substance to which he has become addicted. The addiction clearly has a chemical as well as a neural basis.

CONCLUSION

The total intake of a substance per day is assuredly an important measure for the science of nutrition; but in the study of behavior it is misleading to assume that intake measures a single variable called "appetite." Appetite is a genuine determinant of intake, but it is not the sole determinant. Intake depends upon the palatability of the foods, the affective arousal that follows ingestion of certain foods, or being deprived of them, the existing habits and attitudes of an organism, and the chemical state of the organism as determined by its constitution and dietary history. In addition to these factors there are complex physiologic regulators of intake which we have not considered in this paper.

It is here suggested that an appetite (specific hunger) be defined in behavioral terms as an acquired determination to seek out and select a particular nutrient. Further, it is suggested that the psychologic and chemical determinants of the feeding process be studied in relation to each other. Both a chemical and a psychologic approach are required for an adequate analysis of patterns of food preference and addictions.

Finally, it is clear that we cannot rely too strongly upon the wisdom of the body as a guide to correct nutrition. This must be supplemented by the wisdom of the nutritionist based upon years of careful research. But even the wisdom of the nutritionist is insufficient if he fails to take account of the psychologic factors that regulate the feeding process. After the nutritionist has prepared an adequate diet the animal may refuse to eat it, or he may eat excessive quantities and suffer therefrom. Hence the science and art of feeding animals and men must rest upon psychologic principles as solidly as it rests upon the principles of physiology, chemistry, and the science of nutrition.

REFERENCES

1. Stone, C. P. (Ed.): *Comparative Psychology*, 3rd ed. Prentice-Hall, New York, 1951, pp. 73–74.
2. Young, P. T., and Greene, J. T.: Quantity of food ingested as a measure of relative acceptability. *J. Comp. & Physiol. Psychol.* 46: 288, 1953.
3. McCleary, R. A.: Taste and post-ingestion factors in specific-hunger behavior. *J. Comp. & Physiol. Psychol.* 46: 411, 1953.
4. Shuford, E. H., Jr.: Relative acceptability of sucrose and glucose solutions in the white rat. *Doctoral Thesis in Psychology*, University of Illinois, 1955.
5. Editors of Nutrition Reviews: Self-selection of diets. *Nutrition Reviews* 2: 199, 1944.
6. Young, P. T., and Chaplin, J. P.: Studies of food preferences, appetite and dietary habit; III, Palatability and appetite in relation to bodily need. *Comp. Psychol. Monog.* 18: 1–43, 1945.
7. Harris, L. J., Clay, J., Hargreaves, F. J., and Ward, A.: Appetite and choice of diet; the ability of the vitamin B deficient rat to discriminate between diets containing and lacking the vitamin. *Proc. Roy. Soc. London*, Series B. 113: 161, 1933.
8. Scott, E. M., and Quint, E.: Self selection of diet; III, Appetites for B vitamins. *J. Nutrition* 32: 285, 1946.

9. SCOTT, E. M., and VERNEY, E. L.: Self selection of diet; VI, The nature of appetites for B vitamins. *J. Nutrition* 34: 471, 1947.
10. YOUNG, P. T., and FALK, J. L.: The acceptability of tap water and distilled water to nonthirsty rats. *J. Comp. & Physiol. Psychol.* 49: 336, 1956.
11. YOUNG, P. T.: Studies of food preferences, appetite and dietary habit; VIII, Food-seeking drive, palatability and the law of effect. *J. Comp. & Physiol. Psychol.* 41: 269, 1948.
12. HEBB, D. O.: *The Organization of Behavior.* John Wiley & Sons, Inc., New York, 1949, pp. 200–206.
13. YOUNG, P. T., and RICHEY, H. W.: Diurnal drinking patterns in the rat. *J. Comp. & Physiol Psychol.* 45: 80, 1952.

The Repetitive Element in the Diet

By Paul S. Siegel, ph.d.*

Dr. Brožek has expressed the hope that the symposium will answer two questions, (1) "What's cooking?" and (2) "Where do we go from here?" With this in mind, I should like to review a series of studies, all of which are concerned, directly or indirectly, with the problem of monotony as it is found in the human eating situation. The time and space allotted dictate the omission of detail and a brevity of style that invites communication failure. The risk is taken with the conviction that the objectives of the symposium are best realized by throwing into the hopper as many ideas as possible.

First, let me summarize the results of what might be termed our basic study of eating monotony, an experiment in which 79 college men subsisted for a period of 22 days on a repetitive diet consisting of but two alternate daily menus. Several hypotheses were examined in this experiment. They may be stated briefly as follows. *Monotony is positively related to the number of times a given food item has been consumed. In time, this effect dissipates very slowly or not at all. High initial acceptance slows the growth of monotony. The course of monotony is affected by certain personality factors. And finally, monotony is overtly expressed in lowered food acceptance.* It is readily apparent that monotony is being treated here as an intervening variable in the original Tolman sense,[1] related antecedently to the number of times a food item has been ingested, to its initial acceptance level, and to certain personality characteristics. Behavioral symptoms or consequences may be seen in rating scale changes,[2] in an increase in the amount of uneaten food, and in the refusal to eat.

The following findings lend considerable weight to the original hypotheses:

(1) When a food item is repeatedly eaten, its palatability rating declines.

(2) This decline is greater for ratings assigned by individuals who elect early to discontinue a repetitive diet.

(3) The amount of food left uneaten is greater for individuals who elect early to discontinue a repetitive diet.

(4) Following a decline in the palatability ratings assigned to items comprising a repetitive diet, no recovery to original rating levels comes about with the passage of three to six months' time.

(5) Items of a repetitive diet having an initially high palatability rating show less decline in rating than those rated low initially.

(6) With repeated ingestion, the amount eaten is greater for food items that are rated high initially.

(7) Individuals who assign initially high palatability ratings to items of a repetitive diet will voluntarily persist longer in eating the diet.

(8) Various items comprising a repetitive diet differ in palatability rating decline.

(9) The Otis Test of Mental Abilities and the Minnesota Multiphasic Personality Inventory do not predict period of voluntary participation in repetitive eating.

This paper reports research undertaken in cooperation with the Quartermaster Food and Container Institute for the Armed Forces, and has been assigned number 628 in the series of papers approved for publication. The views or conclusions contained in this report are those of the authors. They are not to be construed as necessarily reflecting the views or indorsement of the Department of Defense.

* Professor of Psychology, the Department of Psychology, University of Alabama, University, Alabama.

Presented at a Symposium on Nutrition and Behavior held at the Laboratory of Physiological Hygiene, University of Minnesota, April 27, 1956, with the cooperation of the National Vitamin Foundation, Inc., New York and under the sponsorship of the School of Public Health, University of Minnesota.

(10) The amount of food left uneaten correlates significantly with palatability rating.

A second study, quite similar in design, is presently underway. The intent is to examine the generality of the above findings. Different menus are being employed and the study provides for comparative analyses among selected canned, frozen, and dehydrated items. Risking later contradiction, it appears at the moment that the original findings are independent of food item type and specification. There is also some reason to believe that dehydrated items are more susceptible to the monotony effect than the canned or frozen counterparts. It is unhappily true that the preparation of dehydrated items is, in part an art. Had the experimenters employed Escoffier as collaborator, the dehydrated items might have suffered less invidious comparison.

What has been herein termed the monotony effect possesses the characteristics of a habit, albeit a negative one. This line of thought introduces the question of where learning enters the picture. It also suggests that we may be concerned here with a narrow aspect of the much broader question of how, in general, we account for the cessation of eating. Certainly our knowledge of internal regulation does not fully explain this behavior.

Professors Richter and Young will surely attest to the fact that the induction of eating is in great part governed by external stimuli. The approach, seizure, and ingestion of food by the adult organism is largely a matter of conditioning, or if you wish, it is a learned response. Incidentally, if this position is pressed to its limit, there is generated the intriguing implication that despite the presence of food, the adult organism will starve to death in a constantly changing environment. It seems entirely proper to inquire if the cessation of eating is also governed, in part, by external stimuli. We postulate that a stimulus pattern consistently associated with the cessation of eating will take on the capacity to evoke stopping eating. It is an obvious implication of Guthrie's contiguity principle.[3] It follows immediately from Hull's conditioned inhibition postulate.[4] It might even be argued from strict reinforcement theory that the cessation of eating more nearly coincides in time with primary reinforcement (the assimilation of nutrients) than does the seizure and ingestion of food. Thus the impulse to cease eating could be more strongly conditioned to the total stimulus situation than the impulse to start eating. This is viewed as a testable hypothesis, and at this writing an exploratory study has been conducted.

We have fed 12 men a repetitive diet in an undeviating routine for a period of 24 days in an effort to build up a strong association between a relatively constant environmental situation and the act of ceasing to eat. On the twenty-fifth day, when the subject reported for supper, he found his place at the table looking much the way it had been when he had last finished eating that particular meal. We had carefully simulated the "look" of used dishes, cutlery, etc. to approximate the visual complex which had been repeatedly associated in the past with the cessation of eating and the condition commonly referred to as satiety. An apology and an excuse were offered the subject and he was invited to sit down in his customary place. Following a delay of two or three minutes, the "used" dishes were removed and replaced dish for dish with the familiar fare. This procedure was repeated on the succeeding evening. If the clinical intuition of an experimentalist may be trusted, the subjects experienced no suspicion of chicanery. No eyebrows were raised. All subjects seemed to accept fully the excuse that another group had been fed earlier.

The records of food intake for the two experimental suppers were pooled and compared with the records of intake for the corresponding "normal" suppers eaten on the immediately preceding and the immediately succeeding evenings (ABBA order). Confirming the hypothesis, food intake for the experimental suppers was mildly but significantly depressed with respect to both bulk and calories. We are now engaged in replicating this study with the pessimism of the man who wears both suspenders and a belt. The second replication may average our results to a zero difference.

Certain controls are lacking in this study and they should be discussed here. As opposed to

learned inhibition, the observed diminution may be attributed to the disturbance of the positive eating response. Perhaps the disruption in the usual routine simply weakened this habit much as the dog's conditioned salivary response is weakened with an incomplete presentation of the exciting stimulus. This was imperfectly controlled. Less disruption of routine was introduced at the control suppers. Also of some concern to this investigator is the absence of a control for "nausea." It may be objected that we are here observing a kind of revulsion arising from the sight of "dirty" dishes. To this point it can be said that the subjects had viewed this scene on many occasions although never immediately before eating. It is also true that the concept of "nausea" is in need of some semantic clarification. If the intended meaning is that of mild aversion to eating, perhaps we are merely employing a different term to describe learned inhibition. If the extreme sense of positive physiologic upset is intended, a control may be found in the results, for no subject showed the profound effect upon intake dictated by this interpretation. Better controls for both habit disruption and "nausea" are planned for the near future.

Finally, let me summarize a recently completed pilot study which stems from the somewhat idle question of what one means when he says, "I am hungry." Or, "not hungry." Or, "tol'ably hungry." Is the individual really sensation oriented in the Cannon-Carlson sense, or is his report strongly influenced by the contemplation of eating a particular food item or items? We have asked a small group of subjects to rate their hunger on a five point scale immediately before eating a strange meal (unknown menu) and immediately before eating a familiar meal. These ratings have been correlated with actual food intake and with palatability ratings obtained following the meal. Although not statistically reliable, the results are encouraging enough to justify a systematic study. In the absence of foreknowledge of the menu, "hunger" correlates about equally with intake and with palatability. When the menu is known beforehand, the correlation with palatability is considerably higher.

It does not seem inappropriate to close this paper with a question or two. Is eating monotony a kind of cultural overlay? Is it peculiar to our western civilization and, possibly, the economy of plenty? One can readily find apparent instances of entire ethnic groups subsisting upon essentially repetitive or monotonous diets. Is eating monotony a particular expression of the broader tendency to seek, sooner or later, variation in an activity? An affirmative answer to these questions carries with it the conviction that ultimately the monotony effect will "fit" into learning theory.

REFERENCES

1. TOLMAN, E. C.: The determiners of behavior at a choice point. *Psychol. Rev.* 45: 1, 1938.
2. PERYAM, D. R., and GIRARDOT, N. F.: Advanced taste-test method. *Food Engineering* 194: 58, 1952.
3. GUTHRIE, E. R.: *The Psychology of Learning.* Harper, New York, 1952, p. 23.
4. HULL, C. L.: *Principles of Behavior.* D. Appleton-Century, New York, 1943, p. 300.

Food Appraisal and Acceptance by Man

THE fortunate combination of words—"Nutrition and Behavior"—has served here to bring together investigators from many different disciplines. The titles of the papers to be presented at this Symposium provide a good sampling of researches on behavior related to food. The behavior of the organism toward food, and the effect of food and the internal environment upon behavior, have come to serve as one of the open channels for the development of understanding among many biologic interests otherwise found in separate, disconnected compartments. The initiator of the Symposium, Dr. Brožek, and the sponsor's representative, Dr. Goodhart, are therefore to be complimented.

This section on *Food Appraisal and Acceptance by Man* could scarcely exist scientifically without the opportunity of being imbedded in such a diorama of specialties. Only by the consideration of the numerous different meanings and expressions of behavior, as to causes and effects, can any common method of appraisal be even entertained.

We already have had the opportunity of hearing the papers presented on the *Impact of Diet on Behavior*, and on *Hunger and Appetite*. These two sections provide us with strong basic evidence from experimental animals of the importance of nutrition in behavior and, again, of the importance of physiologic psychology to the understanding of that behavior.

We therefore are now better prepared to consider extensions of these basic principles as they bear upon food appraisal and acceptance by man. These extensions will include the social and cultural modifiers, recognized by the anthropologist, and factors that must be considered in feeding mental patients. These problems are also the concern of the Armed Forces, in connection with the supply of special items of subsistence for men under severe stress, or isolated, or deprived of normal rations so that special concentrates offer the only nutriment for survival.

The appraisal of foods and acceptance by man must be grounded in sound theoretic considerations, so that we can recognize and separate the major from the minor modifiers. It takes specialists from several different disciplines to provide each of the separate ingredients which come to make up the terms "food appraisal" and "acceptance," and it takes other specialists to tear down the composite of ingredients in the search for some of the important common denominators.

W. FRANKLIN DOVE, PH.D.
Dept. of Public Health
University of Illinois, College of Medicine
Chicago, Ill.

Cultural Factors in Dietary Choice

By DOROTHY LEE, PH.D.

FROM the very first, for the human being ingestion is culturally structured. Is the infant put to the breast, or given the bottle? Will his first suckling be that of colostrum, or of milk, or of some other fluid? Will he be held in a fetal position as he suckles, cradled in naked contact with a mother who curves herself around him, experiencing simultaneously comfort, social warmth, solace, emotional communication and nutrition? Or will he experience his first feeding held in meticulous sanitation against the starched bosom of someone to whom he is merely a case with a name, of someone who regards and expresses this situation as one of sheer nutrition? These questions are answered differently according to the culture of the society into which the infant is born.

The first experience of solid food will differ according to the culture. If he is a Tikopia,[1] he will get premasticated food, warmed with the mother's body-warmth, partly digested through her salivary juices; his mother will put it directly to his mouth with her lips. In our society he will get food with a hard metal spoon, introduced into a mouth which has never experienced anything so solid or hard, into which not even teeth have yet erupted. In all this, the culture enters into the food experience, shaping, emphasizing, even choosing the significant factors for defining that experience. In our own society, we define it—at least academically—as nutrition. Other societies may emphasize the aspect of social sharing to such an extent that nutrition and even the search for satiety may become secondary. Culture may present food mainly as a means for the stilling of hunger, or of getting nutrition, or as the way to psychosomatic health; it may regard eating as a duty or a virtue, or as gustatory pleasure, or as a social or a religious communion. It is the difference in the cultural structuring of the food situation which has made it possible for the people in one urban society to bolt unpalatable food at a quick-lunch counter, while the men of another society, fully as urban, have been prepared to close shop for two hours at noon for the sake of having a leisurely meal at home with their families. The emphasis on the family meal may be so great as to overshadow other aspects. In Athens, during the last war, when the population was starving and cold, soup kitchens were set up by the Red Cross so as to give the people one hot meal a day in a heated room. However, many people asked to be given the food to take home, where they could eat it cold, in a cold room, as a family group. Some of us, in this country, go to great lengths of deprivation and discomfort so as to be able to eat Thanksgiving dinner with our families.

An instance of almost exclusive emphasis on the social aspect of the situation of food ingestion is found among the Arapesh of New Guinea, as described by Margaret Mead.[2–6] Here food and feeding, in its entire process, from production or gathering to consumption, is regarded primarily as a medium for social warmth and intercourse; and this view of food affects the nutritional pattern, as it makes for gross inefficiency from our point of view in food production.

The Arapesh in question live in a mountainous area, so rugged that there is almost no level land, and the small garden plots may be separated by miles of difficult territory from the hamlet. The most economical way to cultivate them would be by one gardener working alone; yet up to six men may work on a small plot,

From the Merril-Palmer School, Detroit, Mich.

Presented at a Symposium on Nutrition and Behavior held at the Laboratory of Physiological Hygiene, University of Minnesota, April 27, 1956, with the cooperation of the National Vitamin Foundation, Inc., New York and under the sponsorship of the School of Public Health, University of Minnesota.

with their wives and children, traveling over forbidding territory from plot to distant plot, enjoying each other's society and the sharing of work. "The ideal distribution of food," writes Margaret Mead, "is for each person to eat food grown by another, eat game killed by another, eat pork from pigs that have been fed by people at . . . a distance."[4] So a man walks miles with his coconut saplings to plant them on the house sites of others, he gives his pigs to relatives in distant hamlets to feed and tend for him, he hunts only to give his kill away, since the lowest form of humanity is the man who eats his own kill, even one tiny bird. Thus it is ensured that every mouthful that the Arapesh consumes has been the medium of social participation.

Here the Arapesh makes a choice which affects his nutrition. His land is thin, his bush inhospitable, the work of getting food very arduous. Yet, instead of concentrating his energies upon procuring all the food possible, the Arapesh dissipate them (or perhaps concentrate them) on the business of including all the social warmth possible within the total food situation. Mead calculated that an Arapesh spends about a third of his time in highly energy-consuming travel, which, from a rationalistic point of view is entirely unnecessary. As a result of all this, the Arapesh are obviously undernourished. Their daily diet consists of less than half of what the government of New Guinea has specified as the minimum for plantation laborers whose life, we gather, is not more arduous than that of the mountain Arapesh at home. Yet, because of their cultural values, these people choose to spend a large proportion of their energy and time on aspects of food that have nothing to do with hunger or nutrition; in fact, if there is "dietary choice" here, it is the choice of malnutrition. The lives of these people, however, belie undernourishment. They live and work happily and reproduce themselves. Mead gives pictures of men walking many miles over very rugged territory to and from their gardens, and working hard when there; of women proudly carrying loads of seventy pounds up and down steep mountainsides.

The Arapesh represent, in their approach to the entire food process, a large number of societies in the Pacific area; societies where, as with the Trobrianders,[6] the main part of the yam harvest was given to the brother-in-law, ideally to function only as gifts and to eventually rot uneaten. These are societies where the exchange of food does not mean the introduction of variety but rather of social intercourse. We have societies where the custom of sharing special or excess food influenced diet in other ways; for example, it meant that no methods of meat preservation were necessary, as with the Ifugao of Luzon;[7,8] here animals were slaughtered only for sacrifice, and the flesh of a large animal would be distributed to all—thus assuring periodic feasts of meat to rich and poor alike.

In considering an individual's reaction to the food he eats, the factor of culture has again to be taken into account. What will whet the appetite, what will bring a feeling of satiety, what is tasty, depends on the particular culture of the individual in question. The Ifugao of Luzon eat sweet potatoes without pleasure; what arouses their appetities is rice. People in the Middle East cannot achieve satiety unless they have eaten bread—with or without accompanying food.

Even what is recognized as food depends on the culture. We do not regard dragon-flies as human food; the Ifugao do.[7,8] They eat three species of dragon-fly, as well as locusts which are boiled, then dried, then powdered and stored for food. They eat crickets and flying ants which they fry in lard. They eat red ants and water bugs and a variety of beetles. I doubt that I would recognize these insects as food, however hungry I might be. On the other hand, I regard milk as food, a fluid which some cultural groups regard with disgust and as akin to a mucous discharge. My culture decides, furthermore, in what form I shall consume my food. As a child in a Greek community, I either drank my milk hot after boiling, or, more frequently, I ate it in the form of cheese or yogurt, but never in the form of cream sauce or an ingredient of bread, as I do in this country. I ate my oranges complete with all the inner skin; I never drank them, nor

ate the segments divorced of their covering. I ate my fruit raw almost always, whether fresh or dried. The food I ate might be regarded as greasy by people of this country, but my bread was not covered by grease, as it is here; except for a few occasions, it was not "bread and butter."

Attempts to introduce the boiling of water in the interest of public health in a Peruvian village[9] met insuperable resistance, because this changed the classification of water from "cold" food to "hot" food; and "hot" food was appropriate only to specific situations. In this area, to understand dietary choice or the preparation of food and the planning of specific menus, it is essential to understand the culturally determined function of "hot" and "cold" foods.

My culture tells me *when to have an appetite for what.* When I get up in the morning, I have no appetite for roast pork, or cold cuts of sausage; but I do have one for ham and fried sausage. For me, this is an appetite acquired gradually over a period of 30 years; before that, according to my Greek urban culture, I would have found ham or eggs or sausages for breakfast revoltingly heavy, whereas I had an appetite for bread and cheese at this time of day. Whether I shall satisfy my appetite or not depends—beyond the economic factor—on culture. Millions of women in this country who have an appetite for rich desserts, for cream in their coffee, for butter on their toast, forego these items in the interest of a slender appearance; we have societies where young marriageable women stuff themselves with equivalent items because their culture sets a value on plumpness.

According to our culture, also, we decide which part of the plant or animal to eat: leaves or flower, or stalk or root; muscle and liver, or the entire animal, including spleen and lungs and intestines, eye-balls and cheeks. Or, according to the culture again, we may have no choice. For example, among the Zulu of South Africa,[10] when a sacrificial ox is killed, a year after the death of the head of the family, the entire kin group assembles, and each individual is given a prescribed part of the ox, according to age, sex, and relationship to the family; need or personal preference are not taken into account.

The cultural influence on food selection may be indirect, representing a value which pervades all areas of living. For instance, in this country monotony of diet has been found to work against appetite. This I believe, is related to the general American value of the new, of change, of variety. We have societies, however, where what is valued is sameness; where monotony is good and sought. And we have societies where the appearance of the staple is necessary and welcome at every meal. A Greek regards bread as appetizing at all meals as well as at snacks; and in this country, where meals often end in sweet desserts, many Greeks take a bite of bread at the very end. Bread has been eaten with every mouthful of food up to dessert; the dessert has been an interruption, a variation of the "monotony," which the eater now proceeds to eliminate, thus leaving the table with the taste of bread in his mouth. In addition, no variety is sought in the kind of bread eaten.

In this country, the emphasis on speed and efficiency throughout the culture has affected dietary choice, for example, transforming oranges into orange-juice, introducing the sandwich lunch; the sandwich form itself is a factor in the selection of foods.

The kind of food appropriate to different occasions during the year, to different days of the week, to different hours of the day, is culturally patterned also. The food of Lent among Orthodox and Catholic Christians, limited to fish and dairy products and vegetable foods, or only to vegetable products; the lamb on Easter or the ham; the Christmas goose; the Thanksgiving turkey; the Sunday dinner; the special Friday evening meal of the Orthodox Jews; the Bairam lamb preceded by the day-long fasts of the Ramadan; duty-days of the Buddhist Burmese which provide festive fare every eight days, and the slim period of the Buddhist Lent which covers one-fourth of the year—all of these dietary "choices" are made for the individual by his culture.

The force of the dietary patterning varies

in the list I have given above. No lamb at Easter may mean only a lack of joy and satisfaction, but lamb accidentally ingested during Lent may mean acute dysphoria to the devout, a sense of sin and perhaps illness. It would be infrinegment of a religious food taboo, and these taboos are a potent selective factor, whether they cover the year or a season, whether they cover a lifetime or a stage of life as with the Murngin of Australia[11] where only men who are fathers can eat porcupine, emu eggs, snake eggs, crayfish and a number of other items. Informants from other societies have reported that they chose starvation rather than infringement of a food taboo, though they obviously lived to tell the tale. Schweitzer[12] presents cases where individuals unwittingly broke a food taboo and died within a day. Such interdictions sometimes deprive individuals of the very food they require. Among the Zulu[10] milk can never be eaten by pregnant or lactating or menstruating women, and preferably never at all past pubescence, as the reproductive function of woman is inimical to the welfare of cattle, and might somehow reach and harm the cattle through the medium of their milk. Besides, people can consume only the milk of the cattle belonging to their own family line, and since women spend their adult lives in the kraal of a different family line, that of the husband, they cannot have milk even when they are not engaged in the reproductive function.

A cultural factor of great importance is expressed in the symbolic aspect of food: in its value to the individual over and above satiation or nutrition. During the last war, after the invasion of the continent, the newspapers announced that whole turkeys had been sent to France, for the Thanksgiving celebration. This, at a time when all conveyance was needed for the final phase of the war effort, gives some clue to the symbolic significance of turkey at Thanksgiving to Americans—not turkey meat, but a whole turkey, to be seen and carved. If the turkeys did arrive, I am sure they contributed strongly to Allied victory. The same turkeys, however, would have been nothing but so much poultry flesh to Greeks or Yugoslavs or Turks at this time, much inferior to mutton.

To people throughout the Middle East, bread is truly the staff of life, having a significance which verges on the religious. In the Egyptian village described by Ammar[13] it is profane to put bread on the ground, all fallen crumbs must be picked up lest they be stepped upon, and any bread that falls on the ground must be kissed before it is removed from harm's way. Here a man heard with horror the tentative suggestion that one could have a meal without bread; and Ammar tells of two women who were divorced by their husbands, mainly for seldom providing them with fresh bread. Here, as in many areas of the Middle East, without bread a meal is impossible, because bread itself is the meal and all "food" is only an accompaniment, something to dip the bread in, or a relish; and satiety, as I mentioned above, cannot be found without bread.

The place which bread holds in the Middle East is held by corn among the Indians of the Southwestern United States and of Mexico; and attempts to enrich the diet in Mexican villages have had to deal with the unshakable place which corn holds in the life of the peasants. In this country, the Hopi say: "Corn is life and piki the perfect food"[14]; and certainly true Hopi life cannot go on without corn. Corn functions as food, but this is only one of its functions. No child can be born with security, nor live through the first hazardous twenty days of life, without corn.[15] The entire process of growing and harvesting corn, in fact, is vital for a meaningful life, since the entire religious cycle of ceremonials is bound with the growing cycle of the corn.[16] In the face of this, "free" rational dietary choice, based on nutritional requirements biochemically determined, has little chance.

Any attempt to affect diet must deal with the cultural factors in dietary choice. It may come to grief against the symbolic value of the food involved. More than this, it must take into account what it is that the food mediates, so as not to destroy values which cannot be replaced with sheer nutrition.

REFERENCES

1. FIRTH, R.: *We, The Tikopia.* A Sociological Study of Kinship in Primitive Polynesia. American Book Company, New York, 1936, p. 139.
2. MEAD, M.: The Mountain Arapesh I. An Importing Culture. *Anthr. Pap. American Museum Natural History* 36: Pt. 3, 1940.
3. MEAD, M.: The Mountain Arapesh II. Socio-Economic Life. *Anthr. Pap. American Museum Natural History* 49: Pt. 3, 1947.
4. MEAD, M.: *Sex and Treatment in Three Primitive Societies.* Part I: The Mountain Dwelling Arapesh. W. Morrow & Co., New York, 1935.
5. MEAD, M. (Ed.): *Cooperation and Competition Among Primitive Peoples.* The Arapesh of New Guinea. McGraw-Hill Book Co., New York, 1937, pp. 20–50.
6. MALINOWSKI, B.: *Coral Gardens and Their Magic,* American Book Co., New York, 1935, pp. 188–239.
7. BARTON, R. F.: Ifugao Economics, University of California Publication in America, *Archael. & Ethnol.* 15: No. 5, pp. 385–446. University of California Press, Berkeley, 1922.
8. MEAD, M. (Ed.): *Cooperation and Competition Among Primitive Peoples.* The Ifugao of the Philippine Islands by I. Goldman. McGraw-Hill Book Co., New York, 1937, pp. 153–179.
9. WELLIN, E.: Water Boiling in a Peruvian Town in *Health, Culture and the Community* (edited by B. D. Paul). Russell Sage Foundation, New York, 1955.
10. CASSEL, J.: A Comprehensive Health Program Among South African Zulus in *Health, Culture and the Community* (edited by B. D. Paul). Russell Sage Foundation, New York, 1955.
11. WARNER, W. LL. *A Black Civilization,* A Social Study of An Australian Tribe. Harper and Brothers, New York, 1937, p. 68.
12. SCHWEITZER, A.: *African Notebook.* Henry Holt & Co., New York, 1939, pp. 57–62.
13. AMMAR, H.: *Growing Up in An Egyptian Village,* Silwa, Province of Aswan. Routledge & Kegan Paul, Ltd., London, 1954, pp. 34, 37.
14. SIMMONS, L.: *Sun Chief,* Yale University Press, New Haven, 1942, p. 52.
15. SIMMONS, L.: *Sun Chief,* Yale University Press, New Haven, 1942, pp. 27–34.
16. THOMPSON, L.,and JOSEPHS, A.: *The Hopi Way.* University of Chicago Press, 1944, pp. 42–43.

The Components of Food Acceptance and Their Measurement*

By FRANCIS J. PILGRIM, PH.D.

MANY FACETS of one's life are related to eating. In addition to its essentiality to health, eating is recognized as a pleasure in its own right. Further, it is not only a personal matter but serves a social function and contributes to interpersonal relationships. Another aspect that must usually be considered either for understanding an individual's eating pattern or for planning group feeding is the economic factor. The planning of a feeding program for a particular group requires knowledge of the patterns of eating behavior of the members of the group. Basically then, we are faced with the problem of predicting the acceptance of foods.

Three things are necessary in order to predict behavior. We must have a criterion, know the components or factors operative in determining the behavior, and have adequate technics for measuring the effects of the components.

CRITERIA

The criteria for establishing the value of a food are different for various disciplines. For the physiologist the nutritional adequacy of the food consumed is the primary criterion while for the menu planner the cost may be an important consideration. The food technologist has other criteria, such as ease of preparation or the keeping quality of the food. For the psychologist, the behavior of the individual or a group, including affective reactions, is the *sine qua non*. In the case of food acceptance, consumption might appear to be the logical and objective criterion, and for many purposes, the operational definition of acceptance, in fact, is consumption. Sometimes we may be interested in nothing more; at other times, consumption may be the only measure which can be obtained. However, in order to include the affective reactions, the criterion of food acceptance should be specified as "consumption with pleasure"—we might say, "the nutrition of body and soul."

COMPONENTS

A "model," or a structure around which to organize the components, should help to systematize the work in this area. It may serve as a guide for establishing testable hypotheses.

The more important components, as we see them at the present time, are illustrated in Figure 1. The words under the heads, such as "internal" or "learning" and "appetite," indicate either the origin of the component or some of the factors that enter into it; other words such as "stimulus," serve only as definitions or explanations. For convenience, each of the three components is shown as contributing its own part to the perception and final acceptance of the food. This does not imply independence of the components; in fact, mutual interactions are known to operate.

Deglutition depends finally on an immediate, favorable sensation; but before one is even tempted to try the food, a number of recent and

From the Quartermaster Food & Container Institute for The Armed Forces, Chicago 9, Illinois.

* This paper reports work undertaken at the Quartermaster Food and Container Institute, and has been assigned number 629 in the series of papers approved for publication. The views or conclusions contained in this report are those of the author. They are not to be construed as necessarily reflecting the views or indorsement of the Department of Defense.

Presented at a Symposium on Nutrition and Behavior held at the Laboratory of Physiological Hygiene, University of Minnesota, April 27, 1956, with the cooperation of the National Vitamin Foundation, Inc., New York and under the sponsorship of the School of Public Health, University of Minnesota.

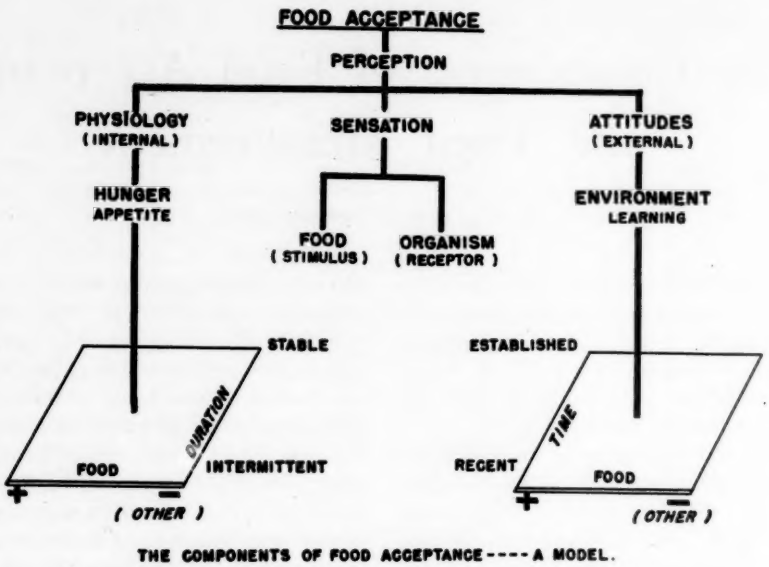

Fig. 1. Relationship Between Methods of Measurement and Components of Food Acceptance.

past events have conspired to influence the organism. Some of the events occur within the individual and others come from the environment. Part of the *milieu* is even non-food in its nature. Both food and non-food factors affecting perception may be recently acquired or long-established, and ingrained. These factors can be represented by points on the planes under PHYSIOLOGY or ATTITUDES (Fig. 1). For example, a relatively stable non-food factor would be endocrine balance; an intermittent food factor would be the metabolic changes following the ingestion of food or the injection of glucose.

An experiment on sensory testing methodology suggests how an important interaction among the factors might occur.[1] The triangle test is used routinely to determine if people can detect any differences in foods due to treatment, source, etc. Two samples are the same and one is different. The subject's task is to indicate which sample is the different one. However, if he is then asked to express his preference between the pair and the third sample an unexpected result may be obtained. If the samples are all the same, or even if the pair has been slightly contaminated with an off-flavor that shows up as a lower preference on a preference test as it is usually conducted, the subject may show a higher preference for the pair than for the odd sample. Now, it is recognized that people often dislike that which is different—the fear of the unknown. This bias is applied to many things in life. The preference results from the triangle test have been interpreted as an effect of this bias. A long standing non-food attitude has altered the perception of the foods that have just been sensed. The sensation and the attitude acted together to produce the effective reaction. We can see that the relative strengths along several dimensions must be known in order to predict whether or not a recent food sensation will take precedence over a long-standing non-food attitude, but one that is able to be generalized to include foods.

METHODS

The methods for the study of acceptance behavior can be grouped for convenience into three classes: attitudes, sensory tests, and consumption. Each of these can be further subdivided into specific technics. Attitude studies can be classified in two dimensions: technic, written or oral; and, population, surveys[2] (general) or case material[3] (particular). Sen-

sory tests are based on two types of response, discriminative judgments and affective reactions, depending on the question asked. The affective reaction is hedonic tone or preference which is the basis of much work in food acceptance. Measurement of the actual consumption of food can be conducted under two conditions, the normal and the experimentally modified. If the latter is more common in animal experimentation, it is only because it is more convenient.

It may be well to outline some of the approaches used at this Institute. For attitude studies we use the survey technics. The most common one[2] is a questionnaire concerned with the degree of preference for each of a number of foods. This is coupled with information on the environmental background of the respondent, including age, region of origin, size of town, length of military service, etc. For some purposes we employ interviews concerning feelings about and knowledge of specific food items. Sensory evaluation of foods involves mainly people's likes and dislikes for samples of foods presented to them in a laboratory setting. Most often these involve preferences for various treatments of the same food item, for example, canned sweet potatoes with different amounts of added sugar or stored for different lengths of time at various temperatures. For special purposes a discrimination test or a flavor analysis, i.e., degree of intensity of specific attributes such as sweet, burnt, musty, etc., may be performed on foods. Preference is not asked for because of the possible biases that could arise. Actual consumption of food has been measured in animals with experimental modification of the diet and with modification of the internal *milieu* by drugs or hormones. In man, consumption has been measured under "normal" eating conditions, and under such conditions as climatic extremes or other stresses, and a restricted number and type of dietary items, such as those discussed by Siegel[4] and by Torrance.[5]

Table I presents our best estimate of the influence of the components of acceptance on the measures obtained with the three methods outlined above. Surveys undoubtedly reflect attitudes previously established; however, we recognize the probable influence of the present physiologic state of the organism on expressed attitudes. For example, in the surveys when the word and not the actual item is the stimulus, soups receive lower preference ratings when the ambient temperature is high than when it is low. The results of sensory tests depend on the immediate sensation produced by the food but the perception of the food is altered by attitudes, both general and food-specific, and by the physiologic state of the individual. Actual consumption will be influenced by the sensations derived from the food and by the physiologic condition of the organism. Past experience or "attitude" may play some role in the case of non-human species; however, in man, one can be reasonably certain that past experience and the attitudes established by them are going to be at least as important as the physiologic state of the person and the sensations elicited by the food. In some cases attitude is the most important factor, as is evidenced by refusal to even sample a food that has never been experienced, i.e., sensed. For example, the idea of eating snails is so repulsive to some people that they refuse to try them.

TABLE I

Relationship Between Methods of Measurement and Components of Food Acceptance

Component	Measurement			
	Surveys	Sensory Tests		Consumption
		Affective	Discriminative	
Attitudes	+++	++	+	++
Physiology	±	+	++	++
Sensation	−	++	+++	++

PROBLEMS

The studies reported in the literature and those now under way or contemplated at this Institute serve to point out some of the prob-

lems that need to be investigated. A few examples of past studies are cited in order to lead up to the problems.

Although we do not yet know which attitudes are most important in determining food preferences, a number of studies have shown, either directly or indirectly, the effects of environment and learning on expressed food preferences, both in surveys and laboratory tests. Surveys of food preferences conducted by this Institute,[2] in which the subjects respond to names and not to the foods themselves, have shown that the respondents' region of origin is related to preferences for many foods. For example, the southeast and southwest are different from the rest of the country. For some foods, age and even the educational level of the respondent seem to be important determiners of acceptance. We have to find out which attitudes are the most important ones, what is their origin and strength, and to what extent they can be modified.

The surveys also suggest that experience in the early years of life, prior to age 16, are among the strongest controlling factors in food preferences. The fact that they appear to be effective determiners of behavior in later life may be a clue to their strength. Yet the work of Lewin[6] and others suggests that food habits are modifiable. The possibility of modifying food attitudes remains as one of the most challenging problems in food acceptance. It would have a special significance for the Armed Services which must feed great numbers of individuals with the minimum of labor and cost. Within the last several years a pilot study was made on the possibility of modifying food attitudes through the use of a mass communication medium, the sound motion picture. This approach looks promising.

The physiologic bases of food behavior have received a good deal of attention over the years, and several approaches are represented by papers at this Symposium. Our organization has been active recently[7] in seeking agents, mainly parasympathomimetic drugs, that increase food consumption. This type of study is just one more way of attacking the problem of the mechanisms regulating hunger and thirst, since it is evident that one or two specifics, such as stomach contractions or blood glucose levels come nowhere near explaining the physiology underlying eating behavior.

An area that demands extensive exploration is that of the effects of stress, including physical exertion, climatic extremes and that most elusive of all, psychologic stress. This area is virgin territory. Unfortunately, there are too few intrepid experimenters who are willing to tackle such problems. If monotony is included as a type of stress, then we can point to two studies.[4,8] However, this research must be recognized as the introduction to a series of investigations that will be required to elucidate the factors that contribute to food monotony.

In recent years, advancements were made in methods for the evaluation of foods on the basis of direct sensory processes. The most useful tool in our own laboratory has been preference measurement by the single stimulus method, using the hedonic scale[9] which is a nine-category continuum from "like extremely" through "neither like nor dislike" to "dislike extremely." However, such a technic does not get at the basis of the differences in preference that arise from processing, storage or other experimental variables. Therefore, we are studying methods of obtaining more analytic data on foods. Flavor analysis appears to offer much promise. However, the greatest obstacle is that we have no adequate system for the description of odors, and odors represent the most important component of most flavors. At the present time we are conducting experiments designed to establish an effective classification system for odors.

PREDICTION

Having recognized the number and magnitude of the variables in food acceptance, it may appear rash to speak of prediction. Nevertheless, we have obtained leads that look promising. It now appears that food preferences, as expressed on a questionnaire, are a fair predictor of consumption. Preference not only predicts the average amount of food consumed in certain situations but also the proportion of persons taking or "accepting" a serving of the food. Because preference, or degree of liking, does predict amounts consumed we can tenta-

tively answer a question raised early in this paper by the definition of acceptance as "consumption with *pleasure*." If we accept "like" as a synonym for pleasure we may conclude that a high correlation between relative preference and amount consumed suggests that the broader operational definition of acceptance has been met, and that preference predicts "acceptance," or consumption with pleasure.

There are numerous problems to be investigated in the three areas of food acceptance outlined in Figure 1. Discovery and integration of the mechanisms by which sensations, attitudes and physiologic phenomena lead to the development of preferences for and behavior toward foods stands as a challenge to research ingenuity.

REFERENCES

1. SCHUTZ, H. G., and BRADLEY, J.: Effect of bias on preference in the difference-preference test. In Peryam, D. R., Pilgrim, F. J. and Peterson, M. S. (Eds.), *Food Acceptance Testing Methodology, A Symposium, Nat. Acad. Sciences–National Research Council*, Washington, D. C., 1954, p. 85,
2. WOOD, K. R., and PERYAM, D. R.: Preliminary analysis of five army food preference surveys. *Food Technol.* 7: 248, 1953.
3. CUSSLER, M., and DEGIVE, M. L.: *'Twixt the Cup and the Lip*. Twayne Publishers, New York, 1952.
4. SIEGEL, P. S.: Repetitive elements in the diet. AM. J. CLIN. NUTRITION 5: 162, 1957.
5. TORRANCE, E. P.: Psychological aspects of ration acceptability. AM. J. CLIN. NUTRITION 5: 176, 1957.
6. LEWIN, K.: Forces behind food habits and methods of change. *The Problem of Changing Food Habits*, Nat. Acad. Sciences–National Research Council, Bull. No. 108, Washington, D. C., 1943, p. 35.
7. SCHUTZ, H., G. and CALLOWAY, D. H.: Reserpine and food intake in the rat. *Fed. Proc.* 14: 385, 1955.
8. PILGRIM, F. J., and SCHUTZ, H. G.: Monotony in food acceptance. *Am. Psychologist*, 1955, 10: 503.
9. PERYAM, D. R., and GIRARDOT, N. F.: Advanced taste-test method. *Food Engineering*, 7: 58, 1952.

Psychologic and Sociologic Aspects of Survival Ration Acceptability

By E. Paul Torrance, ph.d., and Raigh Mason*

Problems concerning emergency rations have stimulated a prolonged controversy. Pemmican, for example, a meat food product currently used in "Ration, Special Survival, RS-1" has been the center of much discussion. Some[1] heatedly maintain that pemmican is unsatisfactory as an emergency ration, much of the justification being based on its low acceptability rating. Others[2] just as heatedly contend that it is the most satisfactory Arctic ration known.

In studies conducted at the U.S.A.F. Survival Training School, no effort has been made to evaluate the adequacy of this product from a nutritional standpoint but to compare its acceptability in a simulated survival situation and what can be done in training to modify the acceptability of the ration. In this paper, we shall summarize the results of three studies thus far directed to this objective.

SUBJECTS

The subjects in all three studies were combat aircrewmen undergoing survival training; the subjects numbered 180, 543 and 429, respectively. Each sample represents a good cross-section of combat aircrew personnel in the U. S. Air Force and includes both officers and airmen.

PROCEDURES

All subjects received a double issue of "Ration, Special Survival, RS-1" supplemented by about 2 lb of beef and a small quantity of vegetables at the beginning of a nine-day simulated survival exercise, about four days of which were spent in a static situation and the remainder in traveling over difficult terrain. One ration included: five meat product bars (pemmican), chili and onion powder, a honey biscuit, a fruit cake bar, eight cubes of sugar, and four packets each of soluble coffee and tea. Subjects in the first and third studies were able to supplement these ratios with such native foods as wild onions, squaw potatoes, blue camus, trout, porcupine, mint, and other foods available in the spring in the Plumas National Forest. The second study, however, was conducted in the winter and little supplementary food was available. The mean temperatures, for the winter exercises were 18.8 and 32.9° Fahrenheit and the mean snow levels were 24.7 and 8.5 in., respectively.

Following the field exercises, all subjects were given a questionnaire to obtain measures of acceptability and provide additional information concerning psychologic, sociologic, and training factors affecting acceptability. The acceptability items included the traditional hedonic scale[3] (9-point in the first and third studies, and 7-point in the second) requiring the subject to indicate his reactions to each of three methods of preparing pemmican, the number of bars of pemmican eaten, reasons for not eating the remainder, and conditions under which the subject would use pemmican in the future.

* Captain, U.S.A.F.

From the Survival Research Field Unit, Air Force Personnel and Training Research Center, Stead Air Force Base, Reno, Nevada.

This report is based on work done under ARDC Project No. 7723, Task No. 77460, in support of the research and development program of the Air Force Personnel and Training Research Center, Lackland Air Force Base, Texas. Permission is granted for reproduction, translation, publication, use, and disposal in whole or in part by or for the United States Government.

Presented at a Symposium on Nutrition and Behavior held at the Laboratory of Physiological Hygiene, University of Minnesota, April 27, 1956, with the cooperation of the National Vitamin Foundation, Inc., New York and under the sponsorship of the School of Public Health, University of Minnesota.

Acceptability indices were obtained according to the following formula:

$$H_1 + H_2 + H_3 + H_4 + P + R(P) + FU$$

where:

- H_1 = Rating on hedonic scale for pemmican eaten cold (1 point for "like extremely," etc.)
- H_2 = Rating on hedonic scale for pemmican heated with water only
- H_3 = Rating on hedonic scale for pemmican heated with water and chili powder
- H_4 = Rating on hedonic scale for pemmican heated with water and onion powder
- P = Number of bars of pemmican not eaten
- R(P) = Reasons for not eating remainder of pemmican (5 points for "made me sick" and one point each for "tasted bad, smelled bad, too hard or dry, or too greasy")
- FU = Condition under which subject would use pemmican in the future (0 for "whenever hungry," 5 for "only when extremely hungry," and 10 for "would not eat even if very hungry")

In the first and second studies, the "favorable" and "unfavorable" groups consisted of the upper and lower 27 per cents on this index. In the third study, the aversion sample was selected by the consensus of two judges and included only those having a clearly and distinctly unfavorable reaction to pemmican. A total of 93 subjects were selected in this manner; the 93 subjects for comparison were selected at random from the remaining cases.

RESULTS

In the first and second studies, the criterion groups were compared by means of the chi-square test computed according to the method described by McNamar.[4] The results are presented in Table I. It will be observed that most of the factors found to be statistically significant in the first study were also found to be significant in the second study. It can be said with reasonable assurance that the following factors are associated with low acceptance:

Prior exposure to unfavorable opinions.

Prior unfavorable expectations or "set."

Perception of unfavorable crew attitude.

More than usual hunger at time of initial use.

Greater amount of time elapsed since last full meal at time of initial use.

Eaten only in small quantities (nibbles) at a time.

First-time use.

Undue fatigue or other unfavorable physiologic condition.

History of present or past food aversions.

In the third study,[5] the mean scores of the acceptance and aversion samples were compared on each of eight scales on the Life Experience Inventory by means of the *t*-test. The results are presented in Table II. Five of the

TABLE I

Factors Associated with Low Acceptability of Pemmican Among Aircrewmen

Factor	1st sample (N = 180)			2nd sample (N = 543)		
	Chi-square	*df*	*p*	*Chi-square*	*df*	*p*
Prior exposure to unfavorable opinions	11.96	3	0.02	2.08	3	0.70*
Prior unfavorable expectations	15.26	3	0.01	13.16	3	0.01
Perception of unfavorable crew attitude	21.36	4	0.001	64.48	2	0.001
Failure of instructor to try to "sell" pemmican as survival ration	6.28	2	0.05	5.20	2	0.20
More than usual hunger at time of initial use	7.68	3	0.05	20.00	3	0.001
Greater amount of time since last full meal at time of initial use	5.20	2	0.07	21.52	2	0.001
Eaten only in small quantities at a time	12.28	4	0.02	26.20	4	0.001
No previous use of pemmican	3.80	2	0.15	7.64	2	0.05
Unfavorable physical condition at time of initial use	2.64	1	0.10	25.52	1	0.001
A relatively restricted diet	31.40	2	0.001	3.16	2	0.30
Food aversions as a child	6.56	2	0.05	5.72	2	0.10
Food aversions at present time	9.40	2	0.01	10.64	2	0.01

* In a third sample, data about prior exposure were collected prior to training and "prior exposure to unfavorable opinions" was found to be significant at the 0.001 level of significance.

TABLE II

Comparison of Life Experience Inventory Score Means of Two Samples of Combat Aircrewmen Divided According to Their Acceptance of Pemmican

Scale	Acceptance group (N = 93)	Aversion group (N = 93)	*t*-ratio	Probability
Motivation	22.43	20.08	2.511	0.05
Leadership	15.34	12.97	2.762	0.01
Adaptability	13.77	12.72	2.360	0.05
Socialized aggressiveness	18.03	15.39	2.938	0.01
Non-conforming aggressiveness	8.18	7.71	0.861	Not significant
Social adjustment	52.61	47.99	2.634	0.01
Risk	21.70	19.80	1.771	0.10
Anxiety	6.52	5.86	1.546	0.15

eight scales differentiate at better than the 0.05 level of significance (motivation for achievement, leadership, adaptability, socialized aggressiveness, and social adjustment).

The detailed item analysis revealed numerous meaningful differences in the life experiences of the two criterion groups under study. One such constellation of items deals with various aspects of willingness to oppose others. Data concerning these items are presented in Table III. It may be inferred from these data that individuals who express an aversion for pemmican characteristically are unable to oppose others by disagreeing, fighting, deviating from norms, or competing. Likewise, they tend not to establish relations with others, or influence and lead them, and are characterized by a pleasure orientation, the association of work with unpleasantness, and overconcern about health.

TABLE III

Comparison of Pemmican Aversion and Acceptance Samples on Items of Interpersonal Aggressiveness and Willingness to Oppose Others

Item	*df*	*Chi-square*	Probability
Frequency of disagreement with teachers*	3	19.35	0.001
Always or usually took a dare	1	4.18	0.05
Fighting as a boy	1	4.88	0.05
Teasing other kids	1	4.52	0.05
Frequency of fighting as a boy	3	12.77	0.01
Frequency of punishment in school	4	5.14	0.25
Frequency of running away from home	3	14.54	0.01
Frequency of wanting to leave home during adolescence	2	11.58	0.01
Rarely or never accepts advice from older people	1	2.75	0.10
Parents disapproved of friends	1	11.37	0.001
Winning in competition important	1	2.65	0.11
Liking for competition	1	3.32	0.07
Improved performance under stiff competition	1	5.28	0.03
Prefers competing against others to competing with own record	1	†	0.01

* In all cases, the greater frequency is for the acceptance sample.

† Probability computed by the "exact method."

Viewed in their totality, the results present a picture of weak ego strength and a relatively unaggressive adjustment to life in general for the aversion sample. Thus, training designed to increase acceptability of survival rations might seek to increase ego strength, to encourage an experimental attitude free of bias, to foster a goal-orientation in adapting to survival rations, and to inform trainees of the scientific facts about the ration.

SUMMARY

Three studies designed to determine some of the psychologic and sociologic factors affecting the acceptability of pemmican in a simulated survival situation were described. In the first, it was found that acceptability was affected by prior exposure to unfavorable opinions, unfavorable personal expectations, perception of crew attitudes, hunger and fatigue at the time of initial use, nibbling only small quantities at a time, and food aversions exhibited presently or during childhood. The second study confirmed most of these and in addition indicated that absence of a prior use of the ration might

be a factor. In the third study, it was found that distinctive patterns of early life experiences differentiate the aversion group from the acceptability group. The acceptability group has had experiences indicative of higher motivation for achievement, more leadership, greater adaptability, a more aggressive adjustment to life in general, and more effective social adjustment.

REFERENCES

1. JOHNSON, R. E., and KARK, R. M.: *Feeding Problems as Related to Environment. An Analysis of United States and Canadian Army Ration Trials and Surveys, 1941–1946*, Quartermaster Food and Container Institute for the Armed Forces, Chicago, 1946.
2. STEFANSSON, V.: *Not by Bread Alone*, Macmillan, New York, 1946.
3. *Food Acceptance Methodology*, edited by D. R. Peryam, F. J. Pilgrim, and M. S. Peterson, Quartermaster Food and Container Institute for the Armed Forces, Chicago, 1954.
4. MCNEMAR, Q.: *Psychological Statistics*, John Wiley & Sons, New York, 1949.
5. TORRANCE, E. P.: *Personality Factors and Survival Ration Acceptability*. Crew Research Laboratory, Air Force Personnel and Training Research Center, Randolph Air Force Base, Tex., 1955. (Technical Memorandum CRL-TM-55-9).

Some Problems of Feeding Mental Patients

HAYDEN H. DONAHUE, M.D., AND PHOEBA A. FOWLER, B.S.

THE need for developing adequate food services in state mental hospitals has been well recognized.[1] In order to assess current practices, the State of Oklahoma made a study of the food purchased for state institutions in the fiscal year, 1952.[2] A committee of the Oklahoma Dietetic Association studied the basic ration plans of some ten states with a view to adopting a standard for Oklahoma. The plan finally established was an adaptation of the U. S. Department of Agriculture *Master food plan at moderate cost.*[3] Table I shows the results of a survey. Column B and C in this table present the standard and the percentages found in 1952 for a typical hospital. At the time of the original study there was no practical way to eliminate data relating to food used in the employee's cafeteria or distributed to some 60 or more families living on the hospital grounds. Information that has become available recently discloses that approximately 12 per cent of the total food budget was spent for employees. The percentages are grossly adjusted in Column D. It can be presumed that the higher-cost foods such as citrus fruits, fresh vegetables, eggs and meats were issued in greater quantities to the employees, thus depleting the patients' supply.

During the past three years a comprehensive treatment program for the mentally ill, including better food service, has been developed in Oklahoma. It involved the placement of qualified dietitians, training of employees, and other improvements. The division of biometrics of the Oklahoma State Department of Mental Health, developed monthly reports on the percentage of each food group currently being used, based on actual store issues for patients only. The standard has been simplified and revised in some food groups. Inspection of the report for October 1955 for the same hospital (Table I) reveals several improvements, the most significant of which are in groups II (citrus and tomatoes), V (other fruits), VI (meats), VII (milk and cheese), and VIII (eggs). The standard for milk has been revised to one quart daily. Groups IX (legumes and nuts) and XII (sugars) have been reduced substantially. It is expected that the high percentage of "other fruits" will compensate somewhat for "other vegetables" in nutrients. Fruits seem to have a better acceptance than the poor quality canned vegetables that are being used. Specifications and methods of purchasing will need to be revised to improve the consumption of vegetables. Group XII (sugars) was reduced by omitting the practice of serving syrup every day for breakfast and jellies at other meals for the sweet or dessert.

The increased percentage of meat represents a much greater amount of edible lean meat. The original study of purchases included carcass beef and pork, whereas the October 1955 study represents trimmed and fabricated cuts ready for cooking. All excess bones, suet and fat are now sold instead of being served as "bony stew" to the patients. Government commodity dried beans and rice are used as potato substitutes, so that the potato level is realistically down. The standard for legumes was revised upward due to their high acceptance. Bread consumption dropped when other foods were offered to the patients. Group XIII shows that a stronger brew of coffee is being made but also indicates that coffee is being served only once daily. Other miscellaneous items in this group are reduced due to accounting procedures of charging other departments for the use of salt, soda, and vine-

From the State of Oklahoma Department of Mental Health, Norman, Oklahoma.

Presented at a Symposium on Nutrition and Behavior held at the Laboratory of Physiological Hygiene, University of Minnesota, April 27, 1956, with the cooperation of the National Vitamin Foundation, Inc., New York, and under the sponsorship of the School of Public Health, University of Minnesota.

gar. Less catsup and pickles are being used, whereas the use of spices and condiments has increased. Government commodity dried beans, rice, beef, dry milk, cheese, and butter affect the October 1955 percentages in a favorable way.

When a new food was to be used or a food not served for years was to be reintroduced, a sufficient quantity was purchased to serve the entire population adequately. To cite an example: the serving of bananas means very little if they are cut into bits and put into a pudding. It may be important to the patients to see and feel a whole banana again. One old man was so impressed that he was moved to tears as he remarked that he didn't know that bananas still grew, then, jokingly, went on to ask whether bananas still grow on trees. When ice cream was re-introduced, the patients ate it in relatively large quantities. Now the consumption has leveled off to a normal serving.

Consumption has been affected by the elimination of greatly disliked and monotonous foods. The high percentage of dried fruits in the original study was principally due to dried black figs. These are no longer purchased. Oatmeal had been served every morning (with the syrup) for years, as far back as menus can be located. Both foods can contribute nutrients to a diet but not when they end in the garbage can.

Thoughtful practices in purchasing and in planning were found to increase food acceptance. Yet, dietary factors are not the whole story. Neither the satisfaction of the food service personnel working with the patients nor the response of these mental patients to good food can be shown on statistical reports. Fights in the dining room, for example, are now extremely rare whereas formerly they occurred during almost every meal. Night cries and screaming have also diminished. Dry skin,

TABLE I

Amounts of Foods Used in a Mental Hospital, Oklahoma Department of Mental Health

		Food purchased, fiscal year, 1952			Patient food issued, month of October 1955		
A	Food group	Standard lb per person daily; unless otherwise specified B	Percentage of original standard (unadjusted C	Adjusted percentage (column C less 12% to D employees)	Percentage of original standard E	Revised standard lb per person daily F	Percentage of revised standard G
I	Green and Yellow Vegetables	0.45	70	62	68	0.45	68
II	Citrus and Tomatoes	0.40	33	29	58	0.40	58
III	Potatoes	0.55	57	50	50	0.55	50
IV	Other Vegetables	0.35	84	74	75	0.35	75 | 125
	Other Fruits	0.22	61 | 70	62	206 | 195	0.25	185 |
V	Dried Fruits	0.03	111 |		112 |		
VI	Beef	0.28	39		61		
	Fish	0.043	61		58		
	Fowl	0.121	39 | 50	44	21 | 58	0.65	58
	Pork	0.186	43		57		
	Other	0.021	258		232		
VII	Milk	1.4	112	99	159	2.15	103
	Cheese	0.025	84	74	102	0.025	102
VIII	Eggs	0.71 each	16	14	108	0.125	77
IX	Legumes and Nuts	0.6 az	300	266	193	0.075	97
X	Flour	0.4	97		83		
	Cereals	1.0 oz	68 | 95	84	73 | 82	0.55	
	Cornmeal and Crackers	0.3 oz	128 |		150 |		82
	Other	1.1 oz	98		62		
XI	Butter	0.075	38		137		
	Bacon and Salt Pork	0.025	391 | 100	88	281 | 155	0.15	155
	Other	0.050	51		88		
XII	Sugar	0.125	284	250	158	0.18	110
XIII	Coffee, Cocoa, Tea	0.05	21 | 104	91	62 | 110	0.125	
	Misc. (Spices, etc.)	0.025	270 |		119 |		76

red, swollen joints, dull and lifeless hair, diarrhea, and constipation are not as great problems as formerly. All of these changes cannot be attributed solely to better diet but probably also reflect better medical and nursing care which are a part of the improved treatment program for the mentally ill.

The emotional significance of food is deeply rooted. The infant is first and primarily an orally-motivated being, and eating represents the child's first contact with the reality of the external world.[4] Food which satisfies the pains of hunger also brings awareness of love and security or rejection and hostility, and food retains strong emotional values throughout life.[5] It can and should become one of the important forces in the treatment and resocialization of the patient. Many of the patients are admitted to a psychiatric hospital in a depleted nutritional state, sometimes of long duration. The burden of their problems has interfered with their habits of living and in many cases has decreased their incomes. Several of the psychotic illnesses involve withdrawal from reality, with the result that appetite is greatly affected. Fantasies involving food may produce bizarre eating patterns and attitudes, such as the belief of a paranoid patient that the food is poisoned.

The effect of the increased tensions and anxieties of the mentally ill on their metabolism and utilization of food has not been sufficiently investigated. Crawfis[6] corroborates this by saying: "In addition to alteration of appetite in mental disturbance, it has been suggested that there may be changes in digestion and absorption of food. It is to be hoped that in the near future we will have more research in this field." The following quotations from recent papers indicate the growing interest and recognition of the role of a good food-service program in the mental hospital: "Food is one therapy in a mental hospital that is available for all patients three times a day. As such it becomes an important instrument for the treatment and rehabilitation of the mentally ill."[7] "Food and the manner in which it is served strongly influence the mental and emotional status of the hospital patients. The well fed patient is one to whom psychotherapy can be applied with the best results."[8] "Mental illness is bad enough in itself, it should not be overlaid by nutritional deficiencies."[9]

Food plays an important role in the patient's life. His acceptance of the food and the value his body derives from it is not determined solely by the preparation, appearance and nutrient quality of the food. Patients appreciate new foods, better quality and better prepared foods, and adequate quantities of well-liked foods. They will respond favorably to a wider choice of foods through cafeteria service, to having attractive dishes, as well as to comfortable and attractive dining rooms.[7] However, the emotional setting, which involves the attitudes of the persons feeding the patient, also plays a dominant role.

SUMMARY

Every meal should be recognized as an opportunity for the socialization of the patient. Every personal contact with the patient should represent a positive step in his rehabilitation.[1] Through the use of dietary standards we have effected substantial general improvements in the diet. However, the needs of special groups can not be overlooked. The more closely acquainted the food-service supervisor becomes with these groups, such as the geriatric, orthopsychiatric, and other special patients, the more adequately will she meet their needs. Fundamentally, food service programs should aim to meet the needs of each individual patient.

REFERENCES

1. Bengs, H. A.: The dietitian's contribution in the care of the mental patient. *J. Am. Dietet. A.* 31: 491, 1955.
2. Executive Department, Oklahoma Division of the Budget: *A Survey of the Cost of Food in the Penal and Eleemosynary Institutions of the State of Oklahoma During the Fiscal Year 1952.*
3. Lifquist, R. C., and Tate, E. B.: *Planning Food for Institutions.* Agric. Handbook No. 16, U.S.D.A., Bull. Human Nutrition Home Econ. 1951.
4. Richmond, J. B., and Pollock, G. H.: Psychologic aspect of infant feeding. *J. Am. Dietet. A.* 29: 656, 1953.
5. Pumpian-Mindlin, E.: The meanings of food. *J. Am. Dietet. A.* 30: 576, 1954.

6. CRAWFIS, E. H.: The dietitian in the mental hospital. *J. Am. Dietet. A.* 30: 464, 1954.
7. OWENS, L., and WHITE, G. S.: Observations on food acceptance during mental illness. *J. Am. Dietet. A.* 30: 1110, 1954.
8. CHAMBERS, B. M.: Food service should be a medical responsibility. *Mental Hosp.*, 5: 17, 1954.
9. HEABERLIN, E.: Nutrition programs in state institutions. *J. Home Econ.* 11: 669, 1955.

Satiety and Weight Control

THE title of this session, "Satiety and Weight Control" is particularly apposite, in that it emphasizes the crucial relevance of the concept of satiety to the problems of overweight. As neurophysiologists, we are of course interested in *hunger* as an essential metabolic and behavioral complex present in all animals endowed with a nervous system. Psychologists are interested in hunger as a "basic" drive. On the other hand, in practice it is *satiety*, rather than hunger which should be the object of our special attention as practical nutritionists concerned with obesity.

There is an obvious reason for this emphasis. Irrespective of the degree of their hunger, modern westerners sit down for meals three times a day. The pattern of the meal is usually pre-set and the main element of choice is in the determination of the size of the portions and the decision as to whether to take second portions. This in turn means that the crucial aspect in controlling intake in our present culture is not the initiation of feeding behavior but its cessation. There are other reasons, however, to emphasize satiety in weight control. Such reasons are physiologic, psychologic, and social. The *physiologic* reasons follow from results expounded elsewhere in this symposium by my co-worker, Dr. Anliker. These indicate to us that the regulation of food intake resides in the application of a brake, sensitive to metabolic influences, of which an essential component is situated in the ventromedial hypothalamic area. This brake slows down or inhibits the operation of a constantly activated feeding mechanism of which a component is probably situated in the lateral hypothalamus. Metabolic influences adjust intake to requirements by acting on the ventromedial area and "modulating," so to speak, this inhibition. Thus what is regulated, in the proper sense of the term, is not hunger, but satiety. To be sure, a number of physiologic and psychologic factors act on the feeding mechanism to inhibit or to facilitate feeding behavior but there is no evidence that such factors are regulatory, i.e., that they contribute to homeostasis.

My associates and I have suggested previously a possible "glucostatic" mechanism for the mediation of the influence of metabolism on the ventromedial area of the hypothalamus. Such a hypothesis is supported by recent work on the specificity of goldthioglucose in causing ventromedial area lesions as well as by the behavioral and physiologic effects of such lesions. It is also supported by the impressive evidence gathered by Dr. Stunkard and his co-workers as regards the action of glucagon and of glucose infusion on gastric hunger contractions and hunger feelings.

A mechanism as complex as the one which recent findings unfold for the regulation of food intake can go wrong in a number of places. All of us have been for a long time familiar with the idea that lack of appetite could be the result of a number of unrelated causes. We are coming around to the idea that the same situation exists as regards hyperphagia. The etiologic points of view can be developed, with consideration of the genetic,

traumatic, and environmental factors in the etiology of obesity. Or the mechanism of the development of obesity—its pathogenesis—may be stressed and one may distinguish between "regulatory" obesities (where the error lies in the central nervous mechanism concerned with satiety and hunger) and "metabolic" obesities (where the primary peripheral abnormalities are followed secondarily by hyperphagia). Among "regulatory" factors, *psychologic* factors are of special importance in the human species. Dr. Charlotte Young, who has been working on the problem of obesity for a considerable time will share some of her observations with us on this point.

Finally there are *social* reasons for the emphasis on satiety. Society brings to bear on the individual a number of important pressures. Advertising is one to which present-day Americans are subjected daily. Popular thinking about food is influenced much more by daily ads, found in all mass media, than by occasional articles or lectures given by nutritionists. For a time, the interests of the food industries coincided almost completely with the viewpoint of public health. It was important to have the population consume a more varied diet and increase its consumption of "protective foodstuffs," fruits, vegetables, milk, etc. Thus advertising conditioned the public to devote a greater amount of money to the purchase of good sources of minerals and vitamins. With the ever increasing prevalence of overweight and the recognition that certain dietary factors may play a major role in the development of arteriosclerosis, we must re-examine the situation. One cannot consume indefinitely more milk, eggs, meat, etc., and not increase the fat content of the diet. In effect, bacon, fried foods, shortenings, large amounts of refined carbohydrates, etc., have no place in the diet of the overweight person. The relevance of these facts to this symposium is that nowadays the advertising seems directed largely toward, precisely, the importance of satiety feelings in weight control. Refined sugars, fats—the emptiest calories from a nutritional viewpoint—are advertised because of their satiety value. This conflict is reflected in the confused thinking of many obese sufferers who, literally do not know any more what to believe about foods. Nor is this situation eased by the frequently punitive tone of many public-health writers, their half-veiled contempt for the overweight subject, and their refusal to recognize with Dr. Young that obesity is a medical, not a moral problem, requiring understanding, patience, and clarity. An obese patient may already have some idiosyncrasies, but added man-made effects may result in more serious secondary disturbances, if not, as Dr. Stunkard has pointed out elsewhere, in actual iatrogenic syndromes. This unraveling of primary psychiatric traits and of secondary disturbances brought about by social premises is going to be dealt with by our other two speakers. Dr. Hilde Bruch, undoubtedly the outstanding specialist on the psychiatric aspects of obesity, is going to speak on the emotional significance of the preferred weight; and Dr. Robert Suczek, whose work on the psychologic typing of obese subjects has attracted wide attention, will speak on the personality of the obese patient.

JEAN MAYER, PH.D., D. SC.
Associate Professor of Nutrition
Harvard School of Public Health, Boston

Psychologic Factors in Weight Control

By CHARLOTTE M. YOUNG, PH.D.,* KATHLEEN BERRESFORD, M.S.,† and NORMAN S. MOORE, M D.‡

MY ROLE here today is not entirely a comfortable one, for I am not an experimental psychologist, a neurophysiologist, an anthropologist, a clinical psychologist, or a psychiatrist. I come as a nutritionist with a practical dietetic background supplemented with training in laboratory research. My interests are definitely in the applied field and primarily in human studies. Perhaps the greatest contribution a nutritionist can make to this group is a statement of her increasing recognition of the tremendous role played by psychologic, cultural, and sociologic factors in the feeding of people. It is well known to any of us who work in the field of human nutrition that our theoretical knowledge of the biochemistry and physiology of nutrition far outstrips the application of this knowledge to the welfare of human beings. There is great need for more cooperative thinking and working between social and biologic scientists on the problems incidental to achieving a better nourished population. We need more biologists who recognize the significance of psychologic influences on every physiologic process in the integrated individual; equally we need more psychologists and social scientists who understand our bungling appreciation of what they have to offer, who will meet us at least half way, in seeking more realistic solutions of our problems.

From the Graduate School of Nutrition, Cornell University, Ithaca, N. Y.

* Professor of Medical Nutrition, Graduate School of Nutrition, Cornell University.

† Formerly Assistant Professor, Public Health Nutrition, Graduate School of Nutrition, Cornell University.

‡ Professor of Clinical Medicine, Graduate School of Nutrition, Cornell University.

Presented at a Symposium on Nutrition and Behavior held at the Laboratory of Physiological Hygiene, University of Minnesota, April 27, 1956, with the cooperation of the National Vitamin Foundation, Inc., New York and under the sponsorship of the School of Public Health, University of Minnesota.

Certainly anyone who has worked extensively with either obese or excessively thin individuals can have no question in his mind but what nutrition and behavior are related. Here behavior affects nutrition leading to over- or under-nutrition, which in turn may lead to further behavior problems. For the past fifteen years we have been working with obese patients.[1,2] At first the work was purely clinical; more recently it has been on a research basis, involving both metabolic and clinical studies. We have learned a great deal about how obese patients act and to some extent how they think and feel. Five studies have been concerned with metabolic responses to weight reduction using carefully supervised dietary regimens.[3–8] A total of 50 obese college men and women have served as subjects. It is in connection with problems which arose in these studies that our interests in the psychologic aspects of obesity crystallized.

METHODS

In the first metabolic study undertaken, the only criteria used in selection of subjects were the following: sufficient degree of obesity; no physical reason for not undertaking weight reduction; and an apparently sincere desire to co-operate in the study. As this initial group contained at least one compulsive eater,[4] it became obvious that these criteria were not sufficient to insure satisfactory subjects. Some means had to be found of selecting individuals who were sufficiently stable to be cooperative. At this point we enlisted the aid of two colleagues in the Department of Clinical and Preventive Medicine: Dr. C. D. Darling, a psychiatrist, and Dr. John Summerskill, a clinical psychologist. Three general questions were raised for discussion: (1) Are all obese persons emotionally unstable? (2) Are there specific personality characteristics which predispose to obesity? (3) Is success in dieting

related to measurable personality factors? The intent of the last question was to see whether by some psychologic instrument one could screen candidates for a controlled weight reduction experiment. At that time six of the ten subjects for the first metabolic experiment were still on our campus. Their co-operation was enlisted in a study undertaken by Drs. Darling and Summerskill and directed toward the three questions listed above.

Each of the women received a one-hour psychiatric interview and three hours of psychologic testing. The purpose of the psychiatric interview was to obtain a rating of the individual's emotional stability, but not to provide therapy or a differential diagnosis as such. Psychologic tests were administered in this order: (a) Thurstone Personality Schedule; (b) Bell Adjustment Inventory; (c) Bernreuter Personality Inventory; and (d) Minnesota Multiphasic Personality Inventory. The psychiatric interview and the psychologic testing were carried out independently and results compared later with the nutritionist's ratings with respect to each subject's performance in the diet experiment.

OBSERVATIONS

Details of the results are reported elsewhere.[9] In general, they indicated that obesity may be associated with varying states of emotional adjustment from essentially normal to seriously disturbed. Also, among the poorly adjusted subjects no single or unique personality pattern was evident either in the psychiatric interviews or by psychologic tests. Findings obtained by psychiatric interview concerning emotional adjustment were in agreement with the findings by psychologic testing. Emotional adjustment scores in turn showed a high positive relationship with dieting performance. Indications were that brief pencil and paper psychologic instruments such as the Bell Adjustment Inventory might be effective in eliminating individuals for whom participation in rigorous dieting could lead to undesirable consequences. The Bell test was selected for further study because of its apparent validity and its ease of administration and scoring.

Our next metabolic study offered an opportunity to examine the use of the Bell Adjustment Inventory as a procedure for selecting individuals suitable for controlled dieting. The nutritionist selected subjects as before, i.e., without regard to emotional status. The clinical psychologist then administered the Bell Adjustment Inventory, and an additional test not used in the previous testing, the Psychosomatic Inventory to the 11 subjects before dieting began. Deliberately, the nutritionist was not informed as to the results. At the end of the experiment, cooperation in dieting was related to emotional adjustment, as measured by the two instruments. Both the Bell Adjustment Inventory and the Psychosomatic Inventory appeared to be highly effective as predictive devices for choosing subjects who could cooperate successfully in controlled weight reduction. This has been reported in the literature[9,10] and since then the two tests have been used successfully in the selection of subjects for three additional metabolic studies of weight reduction of obese college men.[3,7,8]

We also have investigated the feasibility of using the Bell Adjustment Inventory for the selection of obese patients most likely to succeed in weight reduction in a clinic. Perhaps if I tell you about our experiences in the clinic you will see why we were interested in such a device. For some two and one-half years an internist and a nutritionist operated an experimental community nutrition clinic for the express purpose of studying weight reduction. The plan of study and results are described elsewhere.[11] Suffice it here to say that every effort was made to have conditions as conducive as possible to maximum success in weight reduction. The success of our patients in achieving weight reduction was not outstanding; yet it was as good if not better than that of any similar study reported in the literature.

To what was success or lack of success due? In the individual patients, we believed success was related largely to emotional stability and to strength of motivation. Our estimations of emotional stability were made on the basis of rather long and intimate contacts. To us, patients seemed to fall into one of three groups: (1) those who appeared reasonably

stable with few or no emotional problems; (2) those who gave repeated evidence of being tense, anxious or insecure; (3) those who appeared to have deeper emotional problems.

Evaluations of success in weight reduction were made independently by the therapists and then related to a previous independent classification of each patient into one of the three groups listed above. Study of the relationship showed that, in general, patients falling in the first group, the reasonably stable, had a high degree of success in weight reduction. The second group, the moderately tense, anxious or insecure patients, were less successful and what success they had depended on several factors, such as whether or not the patient was able to gain insight into the purpose food served for him, whether he was able to resolve his anxiety, and finally, how strongly he appeared to be motivated. These individuals definitely gained weight during periods of anxiety and tension, either fairly continuously or intermittently when they used food in an attempt to find relief. The third group, with "deeper emotional problems," consisted largely of failures with regard to weight reduction. From this standpoint, therapy was a complete waste of time for them. In some cases, attending the clinic appeared helpful in that various somatic symptoms were relieved without specific treatment and these patients were eager to continue to attend the clinic. In other patients, however, the experience seemed harmful, in that feelings of guilt and frustration appeared to be added to their problems. For the few in the third group who were successful in weight reduction, evidences of emotional instability seemed to be increased. One definitely felt that members of this group should not have been referred to the weight reduction clinic.

Our clinic experience would seem to point to the urgent need for screening of patients, by suitably trained personnel, before they are referred to the usual weight reduction clinic or before a weight reduction regimen is instituted by a physician. If such a screening were made, the frustration of both patient and therapists would be lessened, to say nothing of effecting a great saving in time and money. A psychiatrist or clinical psychologist could make such evaluations. Unfortunately, at least partially because of the lack of sufficient suitable personnel, this is not often done. Hence, the discovery of a pencil and paper test satisfactory for that purpose, which others might use, would be a real help. I should like to tell you of our experience in this direction.

Since the Bell Adjustment Inventory had proven an effective tool in selecting subjects for our metabolic studies, it was decided to include the test in our clinic procedure. Some 90 patients were given the Bell inventory early in their contacts with the clinic and then attended the clinic long enough to make possible an evaluation of their success in weight reduction. The inventories were given, scored, and held in confidence by the public health nutritionist who served as receptionist at the clinic. She had been trained in the administration and scoring of the test by Dr. Summerskill. The internist and nutritionist were not informed as to the test results, with respect to each patient. Later, the success in weight reduction of the patients was evaluated independently, for another purpose, by each of the therapists. At the conclusion of the clinic experiment, the Bell emotional adjustment score of each patient was related to his success with respect to weight reduction—the higher the score, the poorer the subject's adjustment. Table I gives the number of persons falling in each category as well as the mean emotional adjustment score attained by the individuals in each case.

Fifty-two per cent of the patients with above average emotional adjustment were successful in weight reduction; another 42 per cent had "some success." In contrast, 64 per cent of those with below average emotional adjustment were totally unsuccessful, only 32 per cent had "some success," and only one patient in this group was successful. For the patients with average emotional adjustment the greatest percentage, 45, had "some success." Further examination of the records of the six individuals who were successful from the average group showed that they all had

TABLE I

Relationship Between Success in Weight Reduction and Bell Emotional Adjustment Score—Nutrition Clinic Patients

Weight reduction	Bell Emotional Adjustment Score						Total Mean score
	Above average		Average		Below average		
	No. of persons	Mean score	No. of persons	Mean score	No. of persons	Mean score	
Successful	16	3.2	6	9.3	1	18.0	5.5
Some Success	13	3.1	17	11.7	7	19.9	10.3
Unsuccessful	2	4.5	14	11.7	14	21.3	15.7

reason to be highly motivated; four had physical conditions such that weight reduction made them considerably more comfortable and two, for reasons of prestige, could not have allowed themselves to fail. Further study of the records of the individuals with average emotional adjustment scores leads us to believe that the individuals succeeded largely in proportion to their motivation to lose weight or to the conduciveness for weight reduction of their life circumstances at the moment. During the period of study several members of this group had very trying life situations which the therapists felt interfered with performance. Several had no real desire to lose weight; their physicians had urged them to do so, but personally they were indifferent. Furthermore, in the "unsuccessful" category of the patients with average scores, were at least six individuals whom the therapists felt, from material gathered in therapeutic contacts over many weeks, were definitely unsatisfactory in emotional adjustment. Further investigation showed that the actual Bell scores for several of these individuals were only a point or two above the unsatisfactory range.

DISCUSSION

From our experience in the use of the Bell Adjustment Inventory with clinic patients, it would seem that the test might be quite useful in screening patients to be referred to weight reduction therapy. One might expect those with above average emotional adjustment to be reasonably successful in weight reduction; those with below average adjustment would be likely to be unsuccessful and perhaps better not referred. The group with average emotional adjustment would offer the greatest challenge to the physician or nutritionist. Patients with strong motivation and with good life situations would seem to have a fair chance of some success; conversely those with little motivation and trying life situations would probably not succeed. Those with scores just above the unsatisfactory range probably would not be successful. For patients with average emotional scores just starting therapy, probably an attempt should be made to determine the strength of their motivation, if any, and to help them analyze their reasons for resisting achievement. If this can not be done, probably therapy should not be long continued. We feel an attempt should also be made early in therapy to ascertain immediate life circumstances which might make it inadvisable for patients of only average emotional adjustment to undertake the stress of weight reduction. Certainly our experience with the use of the Bell Adjustment Inventory was sufficiently encouraging to warrant further consideration and study.

So much for our experience with the use of a psychologic instrument for predicting success in weight reduction performance whether in metabolic studies or in the clinic. Before closing, there are two or three additional miscellaneous observations I should like to report. The first is this: Among the 168 obese patients followed in the clinic one could find individuals whose use of food was illustrative of most any of the uses suggested by Bruch,[12] Conrad,[13] Hamburger,[14] and others in the psychiatric literature. However, it is not for a non-psychiatrically trained person to present such case studies but merely to support their observations. We should like to stress again that many apparently well-adjusted

people were found in the obese group we observed. Another point is that in our metabolic studies, even among our emotionally-well-adjusted obese young men who were being reduced on a controlled dietary regimen, adequate in all nutrients except calories, we observed many of the same behavior responses reported in the Minnesota Human Starvation Studies,[15] for example general tiredness; weakness especially in climbing stairs; irritability over minor annoyances such as a slight delay in a meal or a later arrival inadvertently being served first; moodiness; increase in psychosomatic complaints; constant talk about food; great preoccupation with ideal weights and the rate of weight loss; either the gulping down of food or undue prolongation of the meal by nursing each morsel; and tremendous increase in the quantities of tea, coffee, and cigarettes consumed during the periods of caloric restriction. Reactions similar to those reported from Minnesota also were found at the "celebration" banquet at the end of the study when, in spite of all the boasting done in advance about what could be eaten, eyes proved far bigger than stomachs.

Finally, another area of research in the psycho-biologic field has been suggested by results from some of our metabolic studies as well as those of others. In both of our studies in which obese young women served as subjects, as weight reduction progressed negative calcium balances were observed on calcium intakes which had led to retentions in the pre-reduction obese state. Brown *et al.*[16] and Leverton and associates[17,18] have reported similar findings. So far there has been no physiologic explanation. My feeling was that stress of some kind, perhaps on an emotional basis, was involved. Then at the 1955 annual meeting of the American Dietetic Association, Stearns[19] reported metabolic studies with 10 young pregnant unmarried women whose emotional problems varied from none at all to grave distress. When the calcium and vitamin D intakes were ample, calcium retention appeared to vary inversely as the amount of emotional disturbance. Furthermore, Malm and Nicolaysen[20] now have a report in press with evidence that in adult male prisoners the efficacy of calcium absorption seemed to be influenced markedly by the emotional state of the individual. With improvement in the emotional state went improvement in calcium utilization.

These studies open a whole area for further research, both in animals and humans, on the effect of emotional states on the biochemical and physiologic metabolic responses. Coupled with the great need for further understanding of human motivation so evident to one interested in clinical dietetics, nutrition education and food acceptance, there seems to be ample evidence that we have only begun to explore the relationships between nutrition and behavior. Our great need is for more scientists, both biologic and social, who are willing to meet each other more than halfway to cultivate the rich rewards of work in psychodietetics.

REFERENCES

1. Waldner, B., Pilcher, H. L., and Young, C. M.: Twelve years of nutrition counseling in a student medical clinic. *Student Med.* 4: 20, 1955.
2. Young, C. M.: The nutritionist in the Student Medical Clinic. *Student Med.* 1: 25, 1953.
3. Fryer, J. H., Moore, N. S., Williams, H. H., and Young, C. M.: Satiety values of isocaloric diets for reducing (with special reference to the glucostatic theory of appetite control). *J. Am. Dietet. A.* 31: 868, 1955.
4. Young, C. M.: Weight reduction using a moderate-fat diet. I. Clinical response and energy metabolism. *J. Am. Dietet. A.* 28: 410, 1952.
5. Young, C. M.: Weight reduction using a moderate-fat diet. II. Biochemical responses. *J. Am. Dietet. A.* 28: 529, 1952.
6. Young, C. M., Ringler, I., and Greer, B. J.: Reducing and post reduction maintenance on the moderate-fat diet. Metabolic studies. *J. Am. Dietet. A.* 29: 890, 1953.
7. Young, C. M., Empey, R., Serraon, V., and Pierce, Z.: Weight reduction in obese young men. Metabolic studies. *J. Nutrition* (in press.)
8. Young, C. M., Brown, A., and Turk, D.: Metabolic studies during stepwise weight reduction in obese young men. (In progress, 1956.)
9. Darling, C. D., and Summerskill, J.: Emotional factors in obesity and weight reduction. *J. Am. Dietet. A.* 29: 1204, 1953.
10. Summerskill, J., and Darling, C. D.: Emotional adjustment and dieting performance. *J. Consult Psych.* 19: 151, 1955.

11. YOUNG, C. M., MOORE, N. S., BERRESFORD, K., and EINSET, B. M.: What can be done for the obese patient? A report of a study in an experimental clinic. *Amer. Pract. & Digest. Treat.* 6: 685, 1955.
12. BRUCH, H.: Psychological aspects of reducing. *Psychosom. Med.* 14: 337, 1952.
13. CONRAD, S. W.: The psychologic implications of overeating. *Psychiat. Quart.* 28: 211, 1954.
14. HAMBURGER, W. W.: Emotional aspects of obesity. *M. Clin. North America* 35: 483, 1951.
15. KEYS, A., BROŽEK, J., HENSCHEL, A., MICKELSEN, O., and TAYLOR, H. L.: *The Biology of Human Starvation.* Vol. II. Chapter 38, University of Minnesota Press, Minneapolis, 1950.
16. BROWN, E. G., HERMAN, C., and OHLSON, M. A.: Weight reduction of obese women of college age. 2. Nitrogen, calcium and phosphorus retentions of young women during weight reduction. *J. Am. Dietet. A.* 22: 858, 1946.
17. LEVERTON, R. M., and RHODES, H. N.: Nitrogen, calcium, phosphorus and basal energy metabolism of obese college women during weight reduction. *J. Am. Dietet. A.* 25: 1012, 1949.
18. LEVERTON, R. M., and GRAM, M. R.: Further studies of obese young women during weight reduction. *J. Am. Dietet. A.* 27: 480, 1951.
19. STEARNS, G.: The nutritional requirements of pregnancy in adolescence. Abstract of paper given at Am. Dietet. A., 38th Annual Meeting, Oct. 20, 1955.
20. MALM, O. J.: Personal communication to the author, 1955.

The Emotional Significance of the Preferred Weight

By HILDE BRUCH, M.D.*

WEIGHT, for scientific discussion, has been defined in so many different terms, that I hesitate to add one more, the "preferred weight."[1] *De facto*, it is not an addition but a contrast. The existing adjectives, such as "standard," "ideal," "average," "expected" or "predicted" weight, refer to some calculated figure derived through manipulation of large-scale observations. These figures are often presented as a measure of a desirable normality for a given individual, with the implication that calculations are proven facts—something they are *not*.

We all know that people in real life do not follow scientific calculations, but have a stubborn way of clinging to their own figures. It is with this real, individual weight that I shall concern myself. I call it "preferred weight" because it represents the weight the organism, in its mysterious self-regulatory capacity, *prefers* as its pattern of adaptation. It often does not coincide with what *we* prefer, or even with what the individual who carries the excess weight professes to prefer. But it seems to be necessary to consider this true weight. The first step in scientific investigation is the establishment of facts as they are, not as we want them to be or claim that they ought to be.

From the Departments of Pediatrics and Psychiatry, College of Physicians and Surgeons, Columbia University, New York, N. Y.

* Associate Clinical Professor of Psychiatry, College of Physicians and Surgeons, Columbia University, New York, N. Y.

Presented at a Symposium on Nutrition and Behavior held at the Laboratory of Physiological Hygiene, University of Minnesota, April 27, 1956, with the cooperation of the National Vitamin Foundation, Inc., New York and under the sponsorship of the School of Public Health, University of Minnesota.

By way of illustration I wish to describe briefly weight curves of a few overweight individuals who have been exposed to extensive clinical treatment and study.

Figure 1 represents the weight of an Italian boy who came to the attention of Vanderbilt Clinic at 11 years of age with a weight of 265 lb. There were several periods of great loss in weight up to 100 lb, under hospital observation. As soon as he returned to his own home he would not only go back to his former weight but continue to gain at the previous rate. He had been unable to find work on account of this weight. If one connects the high points of this curve it proceeds at a steady rate as if these interferences with the natural pattern had not taken place. This man died at the age of 23 of pneumonia.

The next case (Fig. 2) is that of a young man of Irish descent who weighed 100 lb at eight years of age. There was a short-lived effort at reducing. The family's attitude was: "The bigger he is the better we like it." The second period of reducing was carried out under the threat of sexual maldevelopment, with simultaneous endocrine injections; incidentally, this was done against the advice of the Clinic. In retrospect he referred to this period as "the most miserable time of my life." After puberty the increase in weight proceeded in a way remarkably similar to the average for his height and age. There were a few efforts at reducing, associated with a loss of efficiency and a decrease in well-being. He did not like being so heavy but accepted it as the way he and his family were built. He was successful in his work, married and had two children.

In the following case (Fig. 3) there was marked anxiety about his weight and, even more, about possible sexual maldevelopment.

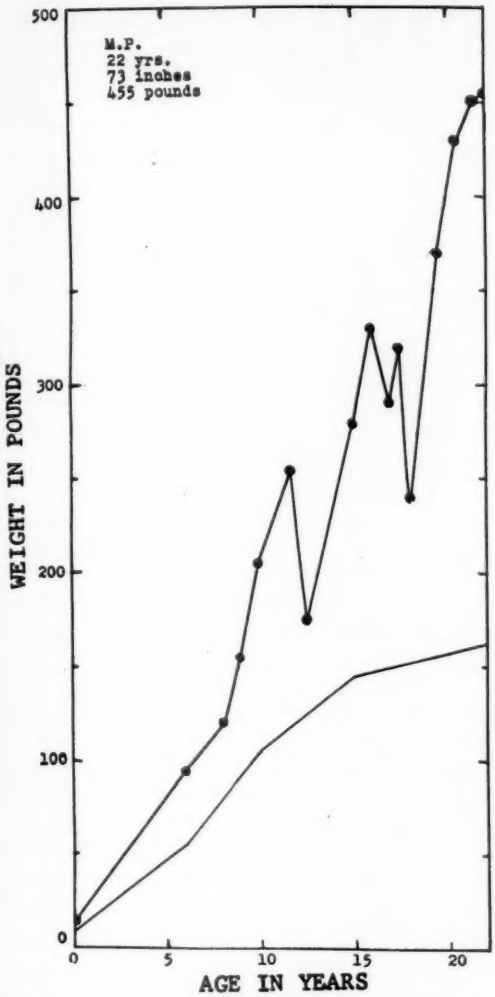

Fig. 1. In this and the following figures the upper, heavy line represents the weight of the patient and the lower, thinner line the average weight for height and age.

There were also many behavior difficulties for which, however, psychiatric treatment was refused. Instead the boy was taken for endocrine injections and he received a variety of products until his entry into the Armed Forces at 19 years of age. The rapid spurt in growth, when he was 10 years old was precipitated by injections of testosterone. While in service he lost 50 lb but had regained

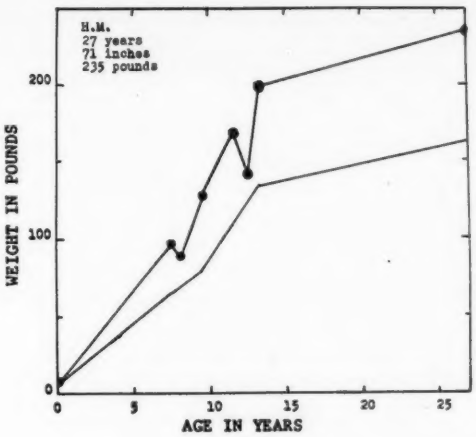

Figure 2

15 lb on his return from Korea. His vocational and social adjustment was marginal.

The case illustrated in Figure 4 represents an example of the always hoped-for "outgrowing" of obesity. During this young man's early life there was much strife between the parents. The mother overpowered the young child with her devoted care and her efforts at keeping him quiet by stuffing him with food. After the family conflicts were resolved, the child was allowed independence appropriate to his age. At no time was food restricted because the mother objected to the very idea of a diet. He had a good high school record, felt socially at ease, and had adjusted well to the Navy, when last heard of.

Figure 5 represents the weight chart of a colored woman who had been a patient at Presbyterian Hospital for the first time in 1917. She had been recently married and moved to New York from one of the Caribbean Islands. She was concerned because she had gained some weight during the preceding months. This was when she was 23 years of age, was 5′ 4″ tall and weighed 148 lb. This was the only time that the patient complained about her weight. She returned to the clinic five years later with a broken finger. Her weight was 196 lb and she reported that it had been 207 lb the year before. From then

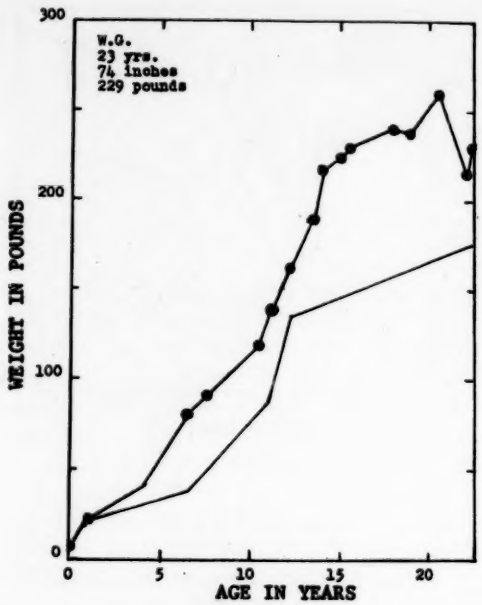

Figure 3

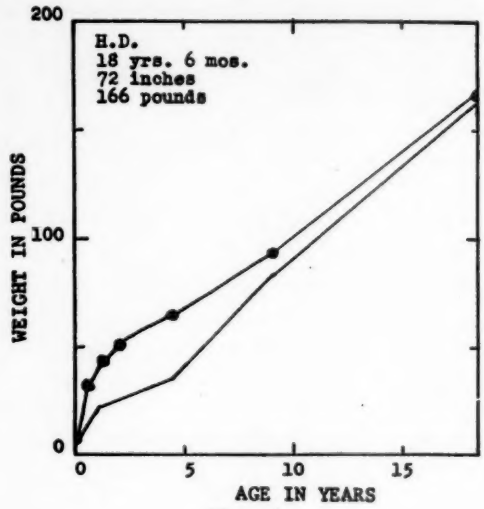

Figure 4

on she came to the clinic for a variety of complaints and minor accidents. When 38 years of age a cholecystectomy was performed after long standing abdomina discomfort. Except for this operation she was sent, for whatever ailed her, to the Food Clinic. She made repeated efforts to follow the prescribed diet and ost as much as 10 or 15 lb. Her lowest weight was 185 lb, one year after the operation, and her highest, two years later, was 220 lb. At that time the patient made a definite statement that she could not diet, that it made her feel weak and irritable. Nevertheless, several more attempts at reducing were made, producing various comments from her physicians about the "hopeless situation" and "the absolutely uncooperative patient." At the last examination prior to some minor surgery, when she was 63 years old, her weight was 198 lb. Otherwise, she was given a clean bill of health. As far as we know she has lived an adequately satisfactory life, having made a new adjustment to the weight she had gained during her early twenties when she moved to New York.

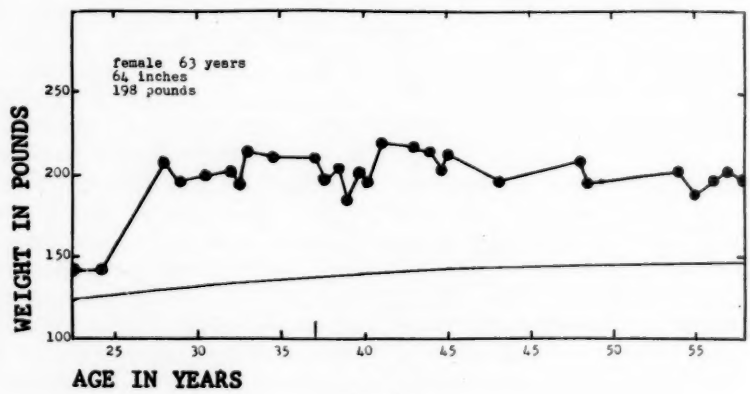

Figure 5

An entirely different picture is represented by the next patient (Fig. 6). Deliberate efforts at reducing, self-imposed by this patient as well as medically supervised, became the outstanding symptom of severe maladjustment. For 20 years he had made many strenuous efforts at reducing, with a total loss of more than 450 lb. He was the youngest child in a large family, more than ten years younger than the next older brother. He had been a fat child but nothing was done about it until he was 16 years old and weighed 265 lb. At that time an older sister took him in hand, insisted on treatment, and supervised his diet during the next year, whereby he lost nearly 100 lb. When he graduated from high school he weighed 169 lb and he felt he was perfect. He considered this year "the golden age" of his life. But he could not maintain the lower weight. Whenever he was confronted with difficulties in his job, trouble with his family, marital difficulties, disappointments during his army career, accidents, etc., he would gain enormous amounts of weight. Any decision to make a new start in life was associated with strenuous reducing at record speed; he would recite the exact figures, like having lost "50 lb in as many days." The hectic weight curve reflects the many shifts in his efforts to find a better adjustment to life. He was haunted by the fear of failure, of not living up to expectations, and the feeling of being an object of ridicule. He sought psychiatric help when it became clear to him that his problems in living could not be solved by reducing.

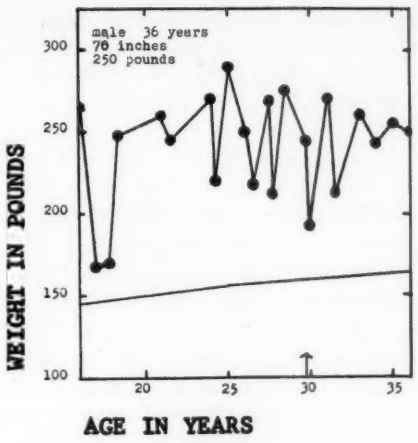

Figure 6

DISCUSSION

These are just a few examples of different patterns in which weight functions in the total adjustment of an individual. To determine the percentage deviation from an assumed normal and to designate a certain deviation as abnormal, is a completely arbitrary and misleading procedure. It says nothing about the competence with which an individual functions. Weight needs to be looked upon, like many other biologic functions (such as gait, pulse rate or manner of speaking) as something which each organism uses in its own preferred pattern. There are wide individual variations in these patterns which, however, are normal constants for a particular individual. Interferences with this preferred pattern, or changes by voluntary decision, result in a sense of discomfort or disatisfaction, a feeling that something is wrong. In weight control this is experienced primarily as chronic hunger with its many by-effects, but also as inability to cope with the stresses of life.

It seems to me an inescapable conclusion that the current approach to the condition of overweight is based on an erroneous assumption, namely, that it is always an abnormal and harmful condition that should or could be removed by dietary restrictions. Whether we like it or not, consider it attractive or ugly, we must recognize it as an undeniable fact that for many people weight is an important factor in their adaptation; it may serve as a protection against more serious illness. There is need to differentiate between overweight that is an expression of a normal variation of body build and that which is pathologic, the expression of a dysfunction, determined by a variety of factors. In either case, interference with the weight pattern of the organism should be preceded by an exact diagnosis of the underlying condition.

There is no doubt in my mind that eventually the physiologists will provide the means of an

exact metabolic diagnosis, or even cure, of the different conditions now lumped together as obesity. Careful clinical evaluation permits classification according to different reactive patterns and thus makes more meaningful treatment possible. This approach is, of course, decidedly less simple than the statistical classification according to percentage overweight; but it has the advantage of coming closer to the true complexity of the problem with which we are confronted. Of greatest importance is an assessment of the psychologic factors that have contributed to the development and maintenance of the excess weight. Their significance can be understood only by relating and integrating them with physiologic data.

I shall focus here only on one aspect, namely, what it means psychologically to have a body weight that is socially and medically condemned as ugly and as indicating self-indulgence and lack of will power. This is painful and embarrassing for an adult. If this social rejection takes place during childhood and adolescence, it has disastrous consequences for the personality development. A feeling of harmony and integrity about one's self and one's body is an important, central experience for a healthy emotional development. The hapless youngster who according to his constitutional make-up is inclined to grow heavy is continusouly exposed to a negative critical attitude and derogatory comments. His concept of self, as well as his body image, is built during childhood from all sensory and psychic experiences. If there is continuous insult to a person's physical make-up, he will be unable to develop a valid feeling of self-esteem and of unity between his psychic and physical self.

The serious and deep-seated emotional disturbances, which are frequently associated with obesity in childhood and adolescence, result not only from the stresses that led to overeating and obesity, but also from psychologic injury to which being fat exposes an individual. It seems to be significant that in the group of fat children followed over 20 years, those had done best in their total adjustment who had been accepted the way they were; the most serious emotional disturbances, including schizophrenic development, were observed in those in whom there had been the most persistent and hostile preoccupation with their weight. For such individuals reducing is commonly recommended as a means of solving their difficulties. The denial of the desire for food, a desire which is deeply interwoven with unfulfilled needs for affection and security, becomes an additional psychologic trauma. In this age of large scale weight control programs, it is necessary to keep the mental health aspect in mind, namely that it is dangerous without having first assessed and corrected the underlying disturbances to interfere with the weight which the organism has used as one of its adaptive patterns.

REFERENCE

1. Bruch, H.: *The Importance of Overweight*, W. W. Norton Co., Inc., New York, 1957.

The Personality of Obese Women

By ROBERT F. SUCZEK, PH.D.*

UNITARY concepts of the cause of obesity are abundant in the literature. The most popular one is that obesity is a matter of overindulgence. The corollary is, of course, that dieting is the only cure. The most recent research and theorizing[1] suggests multiple etiologies and, thus, different types of obesity probably requiring different kinds of treatment.

The major symptom—excessive fatty tissue— is grossly similar from one obese person to another and suggests a unitary disease. Of course, there are differences in the degree of excess fat, and differences in its distribution over the body frame as well. These may be variations in the symptom of the same disease or may represent etiologic differences. Further variations are strikingly apparent in the response of obese people to dieting. The range of results, in terms of weight loss over a given period of time, is as great as degrees of obesity in the obese population. The resistance of the symptom to treatment varies greatly.

Considerations such as these have led to the evaluation of psychologic aspects in terms of two major questions. First, are there some common psychologic characteristics among the obese? Second, are there some psychologic differences among the obese which relate to differences in degree of symptom and differences in ability to reduce?

Research now in progress is aimed at obtaining information relevant to these questions The objective of this paper is to describe some of the leads and suggestions obtained thus far. Details of methodology, statistical procedure and cross-validation of results will be reserved for a later, more comprehensive publication.

From the Department of Research, Herrick Memorial Hospital, Berkeley, Calif.

* Clinical Psychologist, Permanente Psychiatric Group, Oakland, Calif.

Presented at a Symposium on Nutrition and Behavior held at the Laboratory of Physiological Hygiene, University of Minnesota, April 27, 1956, with the cooperation of the National Vitamin Foundation, Inc., New York and under the sponsorship of the School of Public Health, University of Minnesota.

SAMPLE AND METHOD

In connection with the Herrick study of group weight reduction[1,6] a number of psychologic measures were applied to over 300 obese women who volunteered to participate in the experimental weight reduction program. The data to be presented were obtained from a sample of 100 of these women, ranging in age from 18 to 72, with a median age of 42 years. The degree of overweight varied from 5 per cent to 145 per cent, with a median of 41 per cent. The majority of the sample had had their symptom for at least two years and had made at least two serious attempts at weight reduction before.

The psychologic tests used were all group-administered. These included the Minnesota Multiphasic Personality Inventory,[2] the Interpersonal Check List,[3] and ten specially selected Thematic Apperception Test picture.[5] The Interpersonal Check List was used by each subject to describe herself, mother, father, and spouse.

The initial evaluation of these tests was made by using the Interpersonal System of Personality Diagnosis[4] which utilizes eight basic personality variables and achieves a description at several levels of personality; those used in this study include the level of overt behavior, conscious self description, and preconscious fantasy. Other evaluations of the test data are also being used and will be noted in the subsequent sections of this paper. It is recognized, of course, that many other variables must be studied besides those being considered here.

COMMON CHARACTERISTICS

Identification of common characteristics of obese women has been accomplished by a study of their interpersonal attitudes and behavior.[4] In their attitudes about themselves these women are distinguished by an extreme emphasis on psychologic strength, hypernormality, narcissistic pride, and by a denial of weakness. These attitudes would appear to be reinforced by the maintenance of an unusual body size. The obese woman's very dimensions reflect her need for strength and massiveness in order to deny an image of self that is felt to be basically weak, inadequate, and helpless.

The need to maintain a façade of strength and psychologic normality is highlighted by comparison with other symptomatic groups. The obese women are significantly different in their symptomatic behavior from patients in psychotherapy, psychiatric clinic admissions, and hospitalized psychotic patients, all of whom present themselves as weak, dependent, and depressed. In their conscious view of themselves, the obese claim even greater strength than is expressed in their overt behavior and do so to a degree that is significantly greater than in normal control subjects, who in their conscious evaluation of themselves are able to admit to some weakness. Finally, measures of preconscious self-expression, when compared with those of seven other neurotic and psychosomatic symptom groups, place the obese sample closest to the normal controls because of an emphasis on strength and independence.

Thus, viewed as a group, obese women present in common a triple-level façade of power-oriented personality. Compared to other symptom groups, and even to normal control subjects, their narcissistic strength stands out as markedly as does their gross body size.

The power orientation in this sample of obese women is quite consistent. If each subject is given a "diagnosis" of "strong" or "weak" at each of the three levels of self (overt behavior, conscious description, and preconscious fantasy), it is possible to group them according to those who are strong at all three levels, those who are strong at the first two levels and weak at the third, etc., the final group consisting of those who have a "weak" orientation at all three levels. Grouped in this way, 90 per cent of the obese women are in the predominantly "strong" group (i.e., "strong" at all three or at two of the three levels), while, by comparison, only 48 per cent of a sample of psychiatric clinic patients in therapy would be similarly placed. The strength seen in the sample of obese women as a whole is clearly evident in these three separate measures of each individual as well.

Many hypotheses are suggested by this consistent pattern in the obese women. One such is that these people must have special ways of responding to weakness or passivity. An independent evaluation of such a hypothesis is accomplished by study of the responses to card 18GF of the Thematic Apperception Test (TAT), which includes two figures, one generally identified as active, the other as passive. Generally, stories in response to this picture include the identification of the sex of the passive figure. Thus of 47 women psychiatric clinic admissions, 100 per cent gave the sex of that figure, 81 per cent identifying it in their stories as a woman. Of the obese sample, only 83 per cent stated the sex and of those who did, only 66 per cent saw the figure as a woman. These differences approach statistical significance ($P = .10$). Of further interest is the fact that of those obese women who saw the passive figure as a woman, one half of them identified her as a daughter, thus giving her an inferior status. This tendency, compared with the clinic sample, proved to be statistically highly significant ($P = .001$). It would appear that passivity does present some real threat to the obese woman, for she is very reluctant to attribute passivity to one of her own sex, and if she does she rationalizes it by identifying the passive feminine figure as one who is naturally passive or dependent by virtue of her inferior position in the family.

An interesting side light in connection with studies of this kind is that raters reading the fantasy stories written by obese women frequently find themselves bored with them

whereas such fantasy material ordinarily evokes a high level of interest. Subjective evaluation of this rater-ennui suggests that it is related to the rather barren quality of obese women's TAT stories. On the whole they tend to use simple, superficial, and highly conventional themes. Besides lacking in complexity of plot, they have little subtlety or originality of motivation or of character structure. Although the individuals in their stories are expressive of strong emotions, such emotionality seems highly idiosyncratic, or even autistic, having little relationship to the feelings and actions of others in the story. In short, the rigid pattern of strength and hypernormality evident in the interpersonal measures discussed above, is reflected in the fantasy material in the impression of stereotype, barrenness and lack of mutuality or reciprocation in fantasied relationships.

PSYCHOLOGIC DIFFERENCES

The effort to study differences among individual obese women brings up such theoretic and methodologic questions as: what psychologic variables are most relevant to the problem and how can they be measured? An empirical alternative to such theorizing is simply to evaluate two sets of groups which seem to represent functional differences among the obese: (1) the grossly obese compared to the mildly obese and (2) those who lose large amounts of weight in a weight-reduction program compared to those who lose relatively little. Both sets of groups can be easily defined and, if related to important psychologic variables, might provide useful leads for further study and theory.

The first set of groups consists of the 20 least and 20 most overweight subjects in the sample. The range is from 62 to 145 per cent for the grossly overweight and from 5 to 22 per cent for the mildly overweight. The second groups include those who gained weight or lost 10 lb or less in 16 weeks of group weight reduction, and those who lost 26 to 51 lb in the same program.

Degree of Obesity

The primary variable distinguishing the total obese group from other diagnostic groups is the emphasis on strength or interpersonal dominance in their self system. Compared to each other at each of the three levels described above, the 20 least overweight women as a group have lower dominance scores than the 20 most overweight. This trend suggests a consistent association of extreme obesity with high dominance as measured by these technics. Again we see the association of power with the symptom of gross body size.

However, evaluation of the middle group (those who are between 24 per cent and 61 per cent overweight) shows this not to be entirely true. At Level I (overt behavior) the dominance scores of the middle group are even more extreme than those of either the mildly or grossly overweight. At Levels II and III the trend reverses again and the most overweight are the most dominant of the three groups.

Application of statistical measures to these paradoxical differences shows that these trends are statistically significant. Using the measures at Level I, and comparing the combined extreme groups to the moderately overweight group shows the moderates to be significantly higher ($P = .02$) on the measure of dominance. On the theoretic basis that mild obesity may really involve more a problem of body image, while obesity of 30 per cent or greater definitely involves excessive fatty tissue and therefore "true" obesity, a different comparison seems in order. Thus comparing the mild overweights to the medium and grossly overweight, reveals a significantly greater dominance ($P = .05$) on the part of those who are "truly" obese. However, it is already clear that this difference is created mainly by the high scores of the medium group, so the paradox remains. In other studies being done at the present time this same paradoxic trend—for the mildly and grossly obese to be more like each other and different from the middle group on some measures—continues to be apparent. No theoretic or methodologic clarification of this inconsistency has yet been developed.

Another type of study being done involves evaluation of intrapsychic mechanisms used by the obese woman in handling anxiety.

Sorting of Minnesota Multiphasic Personality Inventory profiles into groups which are characterized by the predominant mechanism for handling anxiety has produced four such groups, each with a typical profile:

(*1*) *Internalizer:* The typical neurotic patient using either compulsive, obsessive, phobic or hysterical ways of handling anxiety and with some subjective anxiety, depression and dissatisfaction with self.

(*2*) *Externalizer:* The person who wards off anxiety by repression, denial of feeling, by externalizing problems onto her reality situation, or by acting out anxiety directly in her environment, without any awareness of subjective anxiety.

(*3*) *Schizoid:* The disidentified person who avoids anxiety by being a chronic isolate. She is alienated from her family and her interpersonal community.

(*4*) *Somatizer:* The person who "short circuits" or displaces anxiety into somatic symptoms and a hypochondriacal preoccupation with them.

In the total sample, the first two types are almost equally divided and appear most frequently, together accounting for 67 per cent of the sample.

Comparison of the grossly overweight with the mildly overweight on these variables shows a consistent difference. The heavy group includes a larger number of internalizers (those who are anxious and aware of internal psychological difficulties) and a small number of externalizers (those who are not anxious and externalize their problems). The light group shows the reverse tendency. The other types are evenly divided between the two groups. The trend, then, is for extreme obesity in women to be associated with awareness of internal psychologic problems and with subjective distress related to such problems, while mild obesity is more likely to be related to denial of anxiety and externalization of personal difficulties.

Taking only the extreme groups into account provides us with some leads as to what kinds of factors may be related to the degree of obesity. The most overweight are more power-oriented in their interpersonal orientation and are also more likely to be anxious, introspective neurotics. The mildly overweight, on the other hand, provide a contrasting picture: they have less intense need to be strong, less free-floating anxiety and a tendency to see problems as being external to themselves.

Weight Loss

Study of criteria groups defined in terms of amount of weight loss in a weight reduction program provides a further view of what psychologic variables may be relevant and raises some questions of methodology for future studies.

In comparing good and poor weight losers in terms of interpersonal strength or dominance it was again found that this is a crucial variable, with some relevance to weight loss. In this connection, however, the relationship between dominance scores and pounds lost appears to be more complex than it was found to be in connection with the symptom itself. In general, poor losers tend to have low dominance scores and good losers tend to have scores in the middle range on dominance, but the relationship is a tenuous one. However, if in addition to the dominance score, the degree of overweight is also taken into account, then the relationship between these two variables and weight loss appears to be more consistent. Thus, of the 60 subjects in our sample who are the most overweight (33 per cent overweight or more), those who are heaviest and have consistently higher mean dominance scores lost the most pounds in 16 weeks.

This finding suggests a methodologic change in our approach. Rather than attempting to define some linear relationship between ability to lose weight and a single psychologic characteristic, it is apparent that we must search for combinations of variables that are related to weight loss. The implication of the above study is that such combinations may include not psychologic variables alone but physical or symptomatic variations as well as social or intrapsychic factors.

As an example, we find that identification as reflected in fantasy material may prove to be a relevant factor. Eighty-eight subjects responded to card 4 of the TAT, which pictures

a man and woman in some kind of power struggle. Sixty-six identified the woman in their stories as the hero, while 22 identified the man as the hero. Of those who made the man the hero, a larger number were poor weight losers, while of those who made the woman the hero, a larger number were good losers. The implication here is that for the obese female, an identification with a strong aggressive man is related to resistance to weight reduction, whereas an identification with the feminine figure is related to weight loss.

In short there is some evidence that both amount of overweight and interpersonal dominance are associated with ability to lose weight. Fantasy identification with the same or the opposite sex also seems related. It is evident that ability to lose weight is complexly determined not only by psychologic factors but by physical and possibly by physiologic factors as well. Further study of response to weight reduction programs must be based on a multilevel and multivariable approach to the problem.

SUMMARY AND CONCLUSIONS

Our efforts to study the obese woman's personality are being carried out in relation to two basic questions: what common psychologic characteristics are shared by obese women, and what differences are there among obese women which relate to degree of obesity and ability to lose weight? Thus far there has been consistent evidence of the importance of power in the obese woman's personality and functioning.

A high degree of narcissistic strength and interpersonal dominance is shared by a majority of obese women in our sample, and clearly distinguishes that group from other symptom groups, including psychiatric patients, psychosomatic patients and even, in some respects, normal controls. On the basis of this common characteristic we might generalize about the difficulty that obese women as a group present to any therapeutic effort. Whether faced with psychotherapy or with a weight reduction program, it is highly probable that obese women are apt to enter into an intense power struggle with their therapist, resisting his efforts rather than accepting a mutual responsibility for their treatment.

With respect to personality differences between obese women, and the relationship of such differences to degree of obesity and to ability to reduce, a much more complex problem arises. We find some tendencies for the grossly obese to be the most power-oriented. Among them there are also more of those who are aware of anxiety and of internal psychologic stress. However, these tendencies are not clear cut or consistent and there is repeated evidence in our findings that single psychologic factors may not relate to either the degree of obesity or ability to lose weight. There is also evidence that psychologic factors together with physical factors may, in combination, be meaningfully related to our criteria.

We have, of course, considered only a limited number of psychologic variables, some of which may not be the most relevant to obesity. Other factors of importance may be attitudes relating to orality, including management of oral and other impulses, and use of regressive mechanisms in dealing with psychologic difficulties. Certainly the poor long-range response to a weight reduction program suggests a regressive addiction similar to alcoholism. Other variables may include socio-economic identification and perhaps a host of physical variables as well.

At the present time we are carrying on further studies of such factors as identification (or disidentification) with parental figures as well as further evaluation of sex identification as indicated in fantasy material. The intrapsychic mechanisms for handling anxiety and the degree of anxiety subjectively experienced by the obese woman also offer some promising leads. Finally, in connection with the problem of weight reduction, we have in progress a study on body weight one year following the conclusion of an active weight-reduction program. It seems likely that the most important personality characteristics will be those which differentiate people who are able to maintain a weight loss over a period of a year, from those who regress to their original

weight during the same period of time. Such characteristics should provide us with real insight into the problem of obesity.

ACKNOWLEDGMENTS

This work is being carried on with the active cooperation of the Kaiser Foundation Psychology Research and in particular with Timothy Leary, Ph.D., whose theoretic and methodologic contributions to the research have been invaluable. The author is also grateful to Anne Cassell Apfelbaum for her help in data analysis.

REFERENCES

1. EPPRIGHT, S., SWANSON, PEARL, and IVERSON, C.: (Eds.) *Weight Control*, Iowa State College Press, Ames, Iowa, 1955.
2. HATHAWAY, S. R., and MCKINLEY, J. C.: *The Minnesota Multiphasic Personality Inventory*, The Psychological Corporation, New York, 1951.
3. LAFORGE, R., and SUCZEK, R.: The interpersonal dimension of personality: III. An interpersonal check list. *J. Pers.* 24: 94–112, 1955.
4. LEARY, T.: *Interpersonal Diagnosis of Personality*, Ronald Press, New York, 1956.
5. MURRAY, H. A.: *Thematic Apperception Test*, Harvard Univ. Press, Cambridge, 1943.
6. SIMMONS, W. D.: The group approach to weight reduction. *J. Am. Diet A.*, 30: 437, 1954.

Studies on the Physiology of Hunger

II. THE EFFECT OF THE INTRAVENOUS ADMINISTRATION OF VARIOUS NUTRIENTS ON THE GASTRIC HUNGER CONTRACTIONS OF A MAN WITH SEVERE BRAIN DAMAGE

By ALBERT STUNKARD, M.D.*

With the Technical Assistance of ALBA D. PLESCIA, B.A.

IN 1939 Hetherington and Ranson first demonstrated conclusively that obesity can be experimentally produced by hypothalamic damage.[1] In the few years since then discrete anatomic centers mediating the functions of hunger and satiety have been discovered in the hypothalamus.[2] These discoveries have spurred the hope of finding a relatively simple mechanism whereby caloric balance is maintained, and a search is now under way for some physiologic function which fulfills this regulatory role by activation of the appropriate hypothalamic centers.

Two of the most promising theories concerning the regulation of food intake are the "thermostatic" theory of Brobeck,[3] and the "glucostatic" theory of Mayer.[4] Both of these theories start from the common-sense observation that over a short period of time what will be eaten is in large part determined by what has been eaten, and so, presumably, depends upon some quality of the ingested food. According to the thermostatic theory, "animals eat to keep warm, and stop eating to prevent hyperthermia." The determining factor thus becomes the "specific dynamic action" of the food, and there is evidence that the function of satiety correlates well with the rise in skin temperature which follows the ingestion of food.[4]

The glucostatic theory, on the other hand, holds that the factor responsible for the regulation of food intake is the amount of carbohydrate available for use by the organism. According to this theory, the function of satiety is mediated by hypothalamic "glucoreceptors" which are sensitive to the increased utilization of glucose which accompanies the repletion of carbohydrate stores.

In recent years attempts have been made to validate these hypotheses with results that have been inconclusive and even in conflict.[6–8] Some of these attempts have involved a traditional method of studying (problems of appetite and hunger, measurement of) the gastric hunger contractions.[9,10] This technic provides an objective measure of the hunger state and one which is easily applied to the study of human subjects. Furthermore, it provides a useful if not altogether exact analogue of the processes of hunger and of satiety.

Certain characteristics of the gastric hunger contractions, however, make them unwieldy as a technic for resolving problems raised by the thermostatic and glucostatic theories. In the first place the contractions, like the experience of hunger, are not constantly present, even in the fasting state, but occur periodically, on the average of one half hour out of

From the Study Program in Human Health and Ecology of Man, Departments of Medicine and Psychiatry, New York Hospital-Cornell Medical Center, New York, N. Y.

* Assistant Professor of Medicine, Cornell University Medical College.

This work was supported in part by the Research and Development Division, Office of the Surgeon General, Department of the Army, Contract No. DA-49-007-MD-524.

Presented at a Symposium on Nutrition and Behavior held at the Laboratory of Physiological Hygiene, University of Minnesota, April 27, 1956, with the cooperation of the National Vitamin Foundation, Inc., New York and under the sponsorship of the School of Public Health, University of Minnesota.

every two. Moreover, they are subject to inhibition by a variety of stimuli, most prominently unpleasant sensations and emotions. As a result of their periodicity it is difficult to infuse intravenous preparations of fat, protein, and even carbohydrate rapidly enough to obviate the possibility that any cessation of contractions might be spontaneous, while too rapid infusion is subject to the criticism that such a procedure does not simulate the events of normal satiety. Furthermore, as a result of the susceptibility of gastric contractions to inhibition by emotional influences, it is possible that following the injection of any agent, associated nonnutritional stimuli might lead to gastric inhibition.

Recently it became possible to perform tests of gastric function upon a man with severe brain damage in whom both of these objections were precluded. The results of these tests provide information relevant to current theories of the regulation of food intake.*

DESCRIPTION OF THE SUBJECT

The subject was a 19-year-old man who had sustained severe injury to the cerebral cortex in an automobile accident a year before the present study. He never regained consciousness, and from this time presented the clinical picture of a "decorticate" man. All feeding was administered by stomach tube, and he breathed through a tracheotomy which had been performed soon after his admission to the hospital. Throughout the period of study he received Dilantin® and phenobarbital for the control of atypical convulsive seizures which began shortly after the accident. Periodic urinary and respiratory tract infections had always responded well to antibiotic medication; no tests were performed during any such illness. Small decubitus ulcers made their appearance from time to time and were present during the period of investigation.

In the year following his injury the patient showed slight improvement in the function of his central nervous system. He began to open his eyes, and sometimes they would follow bright objects which were held on his right side. In addition, he frequently showed sucking movements, and these could often be induced by gentle rubbing of the lips or adjacent cheek. Noxious stimulation, such as passing a stomach tube and venipuncture, gave rise to not only a vague withdrawal response but also a reaction resembling sham rage. During such stimulation and for a few seconds thereafter, the patient would scowl, show his teeth and often grind them together, and utter snarling noises. Periods of intense diaphoresis occurred spontaneously several times a day, and lasted from five to ten minutes. Urination and defecation occurred spontaneously.

Upon examination the subject appeared to be an extremely thin, pale, young man lying quietly in bed with no spontaneous motor activity. There were marked flexion contractures with atrophy of all extremities, and generalized hyperreflexia. Abdominal refluxes were absent, and the Babinski sign was present bilaterally; on the right side it was followed by withdrawal of the leg and a mass reflex. As far as they could be tested the cranial nerves showed no impairment except for the inability of the patient to look to the left of the midline.

General physical examination and laboratory tests were negative except for the presence of a small decubitus ulcer and a presumably related mild polymorphonuclear leucocytosis.

DESCRIPTION OE GASTRIC MOTOR ACTIVITY

Description of the gastric motor activity may be sharply divided into two periods, the first one lasting six months, during which the patient was tested on nine occasions, and a second period of two months, during which five tests were performed. The only variable which apparently changed between these two tests was the state of the patient's nutrition, and the differences noted between these two periods are presumably related to this factor. During the first tests the patient was receiving a diet which contained 1400 calories.

* The author wishes to express his graditude for the assistance provided by Dr. Emmanuel Friedman, formerly resident physician at The Veterans' Administration Hospital, Kingsbridge, N. Y., where this study was performed.

contributed by 67 g of protein, 46 g fat, and 179 g carbohydrate. When it became apparent that he was losing weight, six months after testing had begun, the patient was shifted to a diet which contained 3500 calories (230 g protein, 90 g fat, and 440 g carbohydrate). Weight gain began promptly upon institution of this diet, and continued throughout the second series of experiments. These nutritional factors should be kept clearly in mind in evaluating the experimental results.

All tests were performed in the morning following an overnight fast, and were of approximately four hours in duration. Gastric contractions were recorded via a Levine tube with attached gastric balloon. After inflation of the balloon to a pressure of 10 cm of water the tube was withdrawn until resistance was encountered at the cardia, and then the tube was taped into place at the nose. Gastric contractions were recorded on a kymograph by means of a balsa wood float and water manometer. At the beginning of the experiment an infusion of isotonic saline was begun and all injections were given through the tubing in an effort to minimize any effects of the injection procedure upon gastric motility. A control period of one hour always preceded any experimental procedure.

The gastric motor activity of the subject during the first months of testing was of a type which has apparently not been desbribed previously. As soon as the tube was inflated, vigorous gastric hunger contractions began and continued without interruption throughout the several hours of observation. During the entire period when the patient was on a calorically deficient diet the contractions were not interrupted once by the development of either gastric tetany, the so called Type III waves,[11] or by reversion to gastric inactivity or the minimal motor activity described by

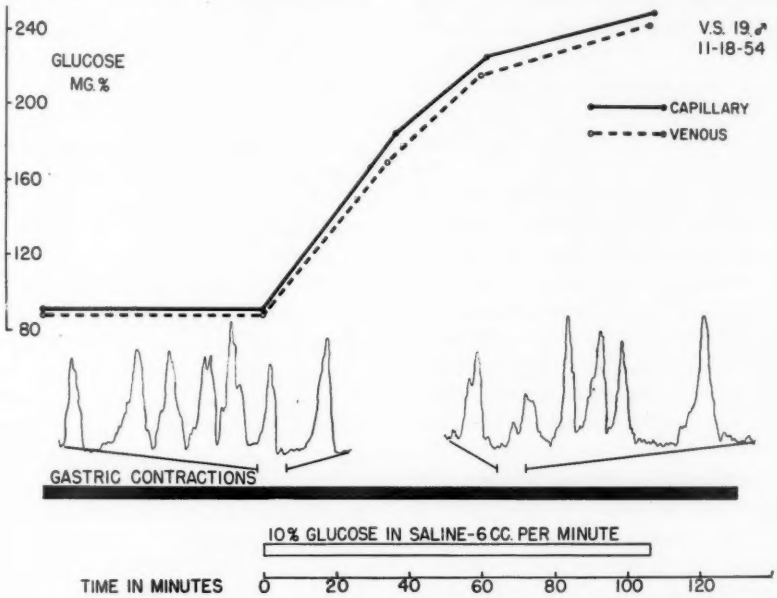

Fig. 1. Persistence of gastric hunger contractions following the intravenous administration of glucose. Infusion of a 10 per cent solution of glucose at a rate of 6 ml per min results in a rise of blood glucose levels to a height of 245 mg/100 ml. Capillary-venous glucose differences remain less than 10 mg/100 ml throughout this time. There is no effect upon gastric hunger contractions.
The sample tracings of gastric contractions are from a kymograph revolving at a speed of one inch per minute. The black bar represents the actual time relations of the contractions to the blood glucose levels.

Carlson as Type I. Graphic illustration of the character of the contractions is provided in Figure 1.

Since the subject was able to respond in a primitive and automatic manner to sensory stimuli it was not possible to predict whether his gastric activity would be influenced by such stimulation. Accordingly, forms of both "pleasant" and "unpleasant" stimulation were used to investigate their influence on the gastric motor activity. As a form of "pleasant" stimulation, the subject's lips were gently rubbed, a procedure which was frequently followed by sucking movements. Such manipulation was never followed by any change in the gastric contractions. Among the forms of "unpleasant" stimulation which were used were venipuncture and inflation of a blood pressure cuff above 100 mm of mercury. Although these usually initiated a withdrawal reaction, and often were accompanied by the previously described pattern resembling sham rage, no effect was noted on the gastric contractions.

Emetic agents are the most powerful central inhibitors of gastric motor activity, and one of the most effective of these is stimulation of the external auditory canal.[12] When the external auditory canal of this subject was irrigated with ice water to the extent necessary to produce nystagmus, no effect on gastric motility was observed.

The absence of spontaneous periods of gastric quiescence as well as the lack of effect of intercurrent stimuli made the subject eminently suitable for study of the effect of the intravenous administration of various nutrients upon the gastric hunger contractions. The persistence of the contractions made it possible to administer the nutrients by means of a constant infusion pump slowly enough to approximate the rate of rise of the concentration of a given nutrient in the peripheral blood during normally occurring satiety.

EFFECTS OF THE INTRAVENOUS ADMINISTRATION OF FAT

The high satiety value of fatty foods is a matter of common experience. It seems most easily explained on the basis of the inhibition of gastric motility by the hormone enterogastrone which is secreted by the mucosa of the upper small intestine in response to contact with fat.[13] Whether or not fat plays a determining role in the overall regulation is not known, but postprandial hyperlipemia correlates to some degree with the function of satiety and it is at least possible that this foodstuff has some central action which may be involved in the regulation of food intake. It was therefore of interest to determine the effects of its intravenous administration upon gastric hunger contractions.

Fat was administered in the form of an intravenous fat preparation "Lipomul"®* which contains 15 per cent (weight/volume) of finely emulsified olive oil in a 4 per cent solution of glucose and water. Such preparations are well utilized by both experimental animals and human subjects. One hundred and twenty ml of Lipomul were administered over a period of one hour at a gradually increasing rate—0.8 ml per min for a period of 25 min, 1.7 ml per min for 10 min, followed by a rate of 3.3 ml per min for a final period of 25 min. The infusion was apparently well tolerated, and there were no signs of any untoward response. At no time either during or after the infusion was there any change in the vigorous gastric hunger contractions.

EFFECT OF THE INTRAVENOUS ADMINISTRATION OF AMINO ACIDS

Following the ingestion of any foodstuff there is a rise in the basal heat production, the so-called "specific dynamic action".[14] It is this increased heat production, manifested also by a rise in skin temperature, to which the thermostatic theory assigns a central role in the regulation of food intake. It is known that the specific dynamic action of the different foodstuffs varies widely. Whereas the proportion of the caloric content of ingested fat expended in heat production is only 4 per cent, and that of carbohydrate is 6 per cent, the corresponding value for protein is about 30 per cent. It appeared that this differential

* Lipomul® was supplied by Dr. Robert W. Heinle, the Upjohn Company, Kalamazoo, Michigan.

might provide a means of testing the thermostatic theory. For the greater heat production of intravenously administered amino acids should have a higher satiety value, and this might be manifested by a greater inhibitory effect on the gastric hunger contractions.

Amino acids were administered in the form of Parenamine,®* a pyrogen-free 6 per cent parenteral solution of casein hydrolysate to which were added all of the naturally occurring and essential amino acids not present in the original hydrolysate. One hundred and fifty ml were administered over a period of 50 minutes. For 20 minutes the protein hydrolysate was given at a rate of 1 ml per minute, and for the next 30 minutes the rate was increased to 4.3 ml per minute. Within 10 minutes after the rate was increased the patient's skin began to flush, and this was followed by profuse diaphoresis. Despite these changes indicative of marked peripheral vasodilatation gastric hunger contractions persisted without interruption.

EFFECT OF THE INTRAVENOUS AND INTRAGASTRIC ADMINISTRATION OF GLUCOSE

In an earlier study the effect of the intravenous administration of glucose on gastric hunger contraction was used as a means of testing the glucostatic theory.[10] Because of the possibility that the disappearance of contractions following injection was due to their normal periodicity, however, it had been necessary to inject the glucose at a rapid and consequently "unphysiologic" rate. The continuous gastric motor activity of the brain-damaged subject obviated this disadvantage and it was possible to infuse a 10 per cent solution of glucose slowly enough to reproduce the postprandial rise in blood glucose levels. The results of such an experiment are illustrated in Figure 1. It can be seen that a rise in blood glucose to a level of 245 mg/100 ml was associated with no change in the gastric hunger contractions.

Although it had been anticipated that this experiment might provide a test of the glucostatic theory, such was not the case. According to this theory, increased utilization of glucose and not the absolute level is the determining factor in the production of satiety. In this experiment such utilization, as inferred from the very small peripheral capillary-venous glucose differences, did not increase, and so no satiety effect would be expected. Alternative ways of increasing glucose utilization were therefore sought.

The intravenous administration of 50 ml of a 50 per cent solution of glucose over a period of three minutes has been found effective in inhibiting the gastric hunger contractions of some subjects with intact central nervous systems.[10] In an effort to increase glucose utilization by a rapid increase in blood glucose levels this method of administration was tried on two occasions. In another two tests such administration was preceded by the intravenous injection of as much as 10 units of insulin, a measure which might be expected to increase the utilization of the glucose. Finally, on the possibility that the intestinal absorption of glucose might alter it in such a way as to promote utilization,[15] it was administered in the form of an intragastric instillation of 500 ml of a 10 per cent solution.

None of these measures sufficed to produce any effect upon the gastric hunger contractions of the subject. Neither did they, however, provide a test of the glucostatic theory. For in none of them was the utilization of glucose increased, as measured by an increase in the peripheral capillary-venous glucose difference. There remains, of course, the possibility that capillary-venous glucose differences measured over a markedly atrophied forearm may not show a significant rise even in the presence of increased peripheral uptake of glucose.

EFFECT OF THE INTRAVENOUS ADMINISTRATION OF GLUCAGON

At this point, when it appeared that none of the currently available methods was able to increase the utilization of glucose in this undernourished man, Van Itallie *et al.* demonstrated that glucagon, the hyperglycemic-glycogenolytic factor of the pancreas, was a

* Parenamine®, a product of Winthrop Labs., Inc., New York, N. Y.

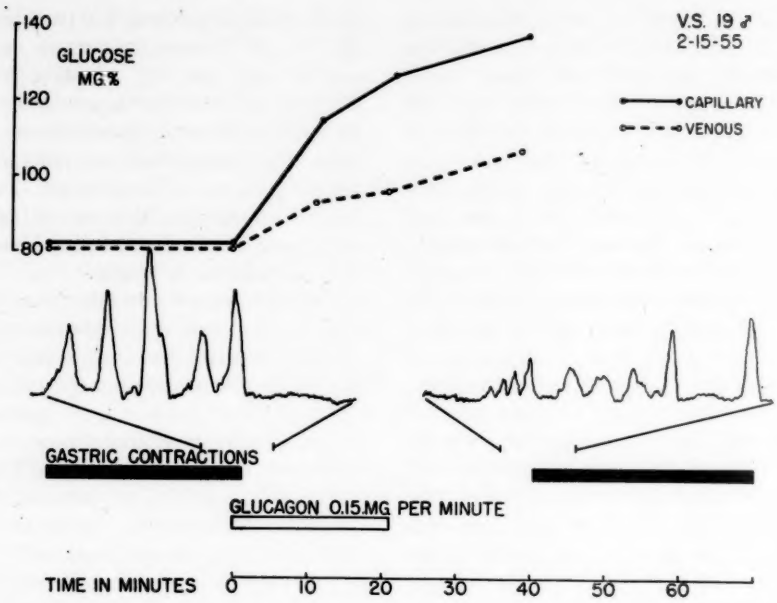

Fig. 2. Cessation of gastric hunger contractions following the intravenous administration of glucagon. Despite the relatively small rise in capillary and venous glucose levels the capillary-venous glucose difference is much larger than after the intravenous administration of glucose.

powerful stimulant to peripheral glucose uptake as measured by peripheral capillary-venous differences.[16] Accordingly, glucagon was administered to the subject by constant intravenous infusion over periods of 20 to 30 minutes, and in doses of 2.0 to 3.6 mg. In each of the four such experiments the results were the same. Gastric contractions were abolished within three minutes of the start of the infusion, and did not return until at least twelve minutes after its termination. Blood sugar determinations performed at intervals before, during, and after the infusions showed a small rise in both capillary and venous glucose levels, and the establishment of a significantly enlarged capillary-venous glucose difference. These findings are illustrated in Figure 2.

RELATION OF THESE FINDINGS TO THEORIES OF THE REGULATION OF FOOD INTAKE

In the present study the gastric inhibitory effects of various nutrients have been compared. Ideally such a comparison would involve similar rates of administration, and, in a study relating to caloric balance, caloric content might be the most suitable basis of comparison. Due to technical considerations, however, the maximal rate of administration of the different nutrients varied in caloric content. The maximal rate of fat infusion was 4.5 calories per minute and that of amino acids 1.0 calories per minute. Use of the 10 per cent solution of glucose yielded a rate of 2.4 calories per minute, whereas the comparable figure for rapid injection was 33.3 calories per minute. It was not possible to determine the rate at which glucose was supplied by hepatic glycogenolysis following the injection of glucagon.

Protein hydrolysate, as measured by its caloric content, was therefore not only infused at a slower rate than fat or carbohydrate, but its maximal rate of administration was less than that following a meal of average protein content. Moreover, the evidence of peripheral vasodilatation cannot be attributed exclusively to the specific dynamic action of the agent; part may well arise from a direct

action on the blood vessel wall.[17] These factors combine to provide a less than ideal test of the gastric inhibitory effect of infused amino acids.

A test of the inhibitory effect of increased glucose utilization was more satisfactory. It was demonstrated that gastric hunger contractions were abolished at the same time that peripheral glucose removal increased, while they were not affected by much higher glucose concentrations which were associated with lesser degrees of glucose removal. These findings appear to support the glucostatic theory and, considered in conjunction with the ineffectiveness of amino acids in similar conditions, provide evidence against the presence of a thermostatic mechanism in these circumstances.

The time relations between the size of the capillary-venous glucose differences and the recurrence of gastric contractions raise a problem which is more difficult to resolve. It has previously been observed[10] that, following the intravenous administration of glucose to normal subjects, gastric hunger contractions ceased concurrently with an increased peripheral uptake of glucose, as is predicted by the glucostatic theory. At the time contractions returned, however, the peripheral uptake of glucose was not significantly lower than it had been shortly after their cessation. Similarly, in the present study, although contractions ceased promptly after the administration of glucagon, in each instance they returned at a time when the presence of still larger capillary-venous glucose differences indicated an even greater peripheral uptake of glucose. These relationships are illustrated in Figure 2. A better correlation exists between the absence of contractions and the duration of the glucagon infusion than between the former and an increased peripheral capillary-venous glucose difference. It is possible that this finding is due to a gastric inhibitory effect of glucagon which is not related to its effects on peripheral carbohydrate utilization. However, in view of the similar finding following the injection of glucose,[10] it would appear that no currently available explanation is adequate.

EFFECT OF POSITIVE CALORIC BALANCE UPON GASTRIC MOTOR ACTIVITY

A month after the subject began to receive a diet which provided a positive caloric balance, and at a time when he was beginning to show definite evidences of weight gain, he was again tested. The pattern of gastric motor activity at this time had changed in the direction of more normal function. Thus, in three of the five tests performed, the subject showed a pattern of alternating gastric activity and quiescence similar to that found in normal subjects. In each of the other two experiments gastric hunger contractions persisted for the entire four hours of the test.

In addition to these changes, formerly ineffective stimuli now became capable of inhibiting gastric hunger contractions. These developments, which were interpreted as representing a decrease in the threshold to inhibition of gastric motility made it impossible to pursue further the current investigation. The unique value of the subject had been due to the unusual stability of his gastric hunger contractions in the presence of the many inhibitory stimuli which presumably are not related to the regulation of food intake. The inhibitory value of the various nutritional agents which *may* be so related could thus be assessed. Reversion to (nearly) a normal pattern of gastric activity brought with it all of the objections to the method which were reviewed earlier. Thus, during this period contractions ceased following the injection of fructose, protein hydrolysate and glucose. It is worthy of note that peripheral-capillary venous glucose differences measured during this latter experiment showed negligible peripheral uptake, and the cause of this inhibition must be sought in sources other than those postulated by the glucostatic theory.

SIGNIFICANCE OF GASTRIC HUNGER CONTRACTIONS IN CALORIC REGULATION

In the present series of investigations the inhibition of gastric hunger contractions has been used as a measure of the function of

satiety. It may be appropriate to consider the rationale of this inference.

Gastric hunger contractions have been used for 50 years in the investigation of problems of appetite and hunger, and during this time views as to their significance have varied widely. The demonstration in the early 1900's by Cannon and Carlson of the temporal correlation of gastric hunger contractions and the experience of hunger led to the hypothesis that the regulation of food intake depended in large part upon the transformation of some physiologic deficiency state into the experience of hunger through the agency of the gastric motility.[11,18] No clear distinction, thus, was drawn between hunger as a sensation and hunger as a drive, although it was tacitly assumed that the latter was mediated by the former. Since the demonstration that animals with denervated stomachs can maintain caloric balance,[19] it has become clear that hunger drive can be entirely independent of that part of the experience of hunger which is mediated by the gastric hunger contractions. Since it is the drive aspect of hunger which is of importance in the regulation of food intake, studies of gastric motility provide only an indirect measure of this most significant function. Even such an indirect measure may, however, be pertinent.

A fundamental response of protoplasm is an increase in irritability as a consequence of the depletion of nutritive stores, and a decrease in irritability with replenishment of the stores. In the higher animals this irritability is focussed in the central nervous system,[20] and one of its most dramatic manifestations is the initiation of the gastric hunger contractions. Such contractions then may be viewed as a localized and highly sensitive index of the general bodily irritability which follows deprivation of food, and their abolition may reflect the decrease in irritability which is associated with satiety. The behavior of the stomach and the behavior of the organism may thus represent parallel responses to nutritional depletion, and the study of one may help in understanding the other, even in the absence of a causal relationship.

SUMMARY

The gastric motor activity of a man suffering from very severe brain damage has been studied under conditions of negative and positive caloric balance. During a time when he was losing weight vigorous gastric hunger contractions persisted without spontaneous interruption throughout the four-hour periods of study. The intravenous administrations of glucose, fat, and amino acids had no effect upon these contractions but they were promptly abolished by the infusion of small doses of glucagon, the hyperglycemic-glycogenolytic factor of the pancreas.

These findings are more readily explained by the glucostatic than by the thermostatic theory of the regulation of food intake. The return of gastric hunger contractions in the presence of markedly increased peripheral utilization of glucose, however, is difficult to explain in terms of the glucostatic theory.

When the subject began to gain weight his gastric motor activity reverted toward the normal pattern although gastric hunger contractions were still present a higher percentage of the time than has been found in individuals without brain damage. At this time several previously ineffective agents were able to inhibit gastric motility.

REFERENCES

1. Hetherington, A. W., and Ranson, S. W.: Experimental hypothalamico-hypophyseal obesity. *Proc. Soc. Exper. Biol. & Med.* 41: 465, 1939.
2. Brobeck, J. R.: The physiology of appetite. Overeating, overweight and obesity. *Proceedings of Nutrition Symposium, Harvard School of Public Health*, National Vitamin Foundation, New York, 1953.
3. Brobeck, J. R.: Food intake as a mechanism of temperature regulation. *Yale J. Biol. & Med.* 20: 545, 1948.
4. Mayer, J.: Genetic, traumatic and environmental factors in the etiology of obesity. *Physiol. Rev.* 33: 472, 1953.
5. Booth, G., and Strang, J. M.: Changes in temperature of the skin following the ingestion of food. *Arch. Int. Med.* 57: 533, 1936.
6. Van Itallie, T. B., Beaudoin, R., and Mayer, J.: Arteriovenous glucose differences, metabolic hypoglycemia and food intake in man. Am. J. Clin. Nutrition 1: 208, 1953.
7. Fryer, J. H., Moore, N. S., Williams, H. H., and Young, C. M.: Satiety value of isocaloric diets for reducing. *J. Am. Dietet. A.* 31: 868, 1955.

8. Bernstein, L. M., and Grossman, M. I.: An experimental test of the glucostatic theory of regulation of food intake. *J. Clin. Investigation* 35: 627, 1956.
9. Stunkard, A. J., Van Itallie, T. B., and Reiss, B.: The mechanism of satiety; effect of glucagon on gastric hunger contractions in man. *Proc. Soc. Exper. Biol. & Med.* 89: 258, 1955.
10. Stunkard, A. J., and Wolff, H. G.: Studies on the physiology of hunger. I. The effect of intravenous administration of glucose on gastric hunger contractions in man. *J. Clin. Investigation* 35: 954, 1956.
11. Carlson, A. J., *Control of Hunger in Health and Disease.* University of Chicago Press, Chicago, Ill., 1916.
12. Wolf, S.: The relation of gastric function to nausea in man. *J. Clin. Investigation* 22: 877, 1943.
13. Grossman, M. I.: Gastrointestinal hormones. *Physiol. Rev.* 30: 31, 1950.
14. Best, C. H., and Taylor, N. B.: *The Physiological Basis of Medical Practice.* 6th ed., Williams and Wilkins, Baltimore, 1955.
15. Scow, R. O., and Cornfield, J.: Quantitative relations between oral and intravenous glucose tolerance curves. *Am. J. Physiol.* 179: 435, 1954.
16. Van Itallie, T. B., Morgan, M. C., and Dotti, L. B.: Effect of glucagon on peripheral utilization of glucose in man. *J. Clin. Endocrinol.* 15: 28, 1955.
17. Macht, M. B.: The effects of various amino acids on peripheral blood flow and skin temperature. *J. Clin. Investigation* 27: 454, 1948.
18. Cannon, W. B., and Washburn, A. L.: An explanation of hunger. *Am. J. Physiol.* 29: 441, 1912.
19. Grossman, M. I., Cummins, G. M., and Ivy, A. C.: The effect of insulin on food intake after vagotomy and sympathectomy. *Am. J. Physiol.* 149: 100, 1947.
20. Sherrington, C. S.: *Textbook of Physiology,* vol. 2, Pentland, Edinburgh, 1900.

Nutrition News

Latest Developments in Fields of Food and Nutrition to Be Discussed at 1957 Gordon Research Conference

The 1957 Gordon Research Conference on Food and Nutrition will be held August 19 to 23 at Colby Junior College, New London, New Hampshire. These conferences, affiliated with the American Association for the Advancement of Science, were established to stimulate research in universities, research foundations, and industrial laboratories. This purpose is achieved by an informal type of meeting consisting of scheduled lectures and free discussion groups. Sufficient time is available to stimulate informal discussions among the members of a Conference.

Among the topics to be discussed are: *Antibiotics in Food Preservation; Advances in Mineral Nutrition; Fat Metabolism and Atherosclerosis; Advances in Protein Nutrition; Nutrition in Liver Disease; Preservation of Food by Ionizing Radiations; Operations Research.*

Attendance at each Conference is limited to 100. Requests for application forms or other information should be addressed to W. George Parks, Director, Department of Chemistry, University of Rhode Island, Kingston, Rhode Island.

Proposed Minimum Requirements for B Vitamins

A proposed regulation establishing new "minimum daily requirements" for two of the B vitamins was published February 16 by the Food and Drug Administration in the *Federal Register*.

This ruling, if passed, would amend FDA's dietary food regulation to fix the adult minimum daily requirement for niacin for the first time. The requirements would be set at 10 mg. The ruling also would reduce the adult minimum daily requirement for riboflavin from 2 mg to 1 mg.

Under such a regulation minimum daily requirements for niacin would be: 2.5 mg for infants; 5 mg for children under six years of age; 7.5 mg for children of six and over; 10 mg for adults.

The revised minimum daily requirements for riboflavin would be: 0.5 mg for an infant; 0.75 mg for a child; 1 mg for an adult.

Wayne University Nutrition Conference

The Third Annual Nutrition Conference, sponsored by Wayne State University College of Medicine, will be held on Thursday and Friday, April 4 and 5, 1957.

The subject for discussion will be "Fats—Helpful or Harmful." Included in the program of speakers are: Drs. John B. Brown, Ohio State University; Frederick J. Stare, Harvard University; Grace A. Goldsmith, Tulane University; and Ancel Keys, University of Minnesota. Further information may be obtained from the Department of Physiological Chemistry, Wayne Study University College of Medicine, Detroit 7, Michigan.

Public Health Traineeships Open

The U. S. Public Health Service announces that traineeships under its program for 1957–58 are available for training all types of professional public health personnel, including physicians, dentists, nurses, and nutritionists. Preference is given to qualified individuals who have had no more than two years' experience in public health work, who have had less than one year of graduate or specialized public health training, and who are under 35 years of age. Stipends covering living expenses for the trainee and legal dependents, as well as tuition and related costs, are included in the traineeship awards.

Applicants may secure application forms and additional information from the Chief, Division of General Health Services, Bureau of State Services, Public Health Service, U. S. Department of Health, Education and Welfare, Washington 25, D. C.

Nutrition Briefs

CURRENT OBSERVATIONS OF CLINICAL INTEREST

VITAMIN B_{12} supplementation (50 μg cyanocobalamin daily for six months) did not have any detectable effect on the growth, general health, susceptibility to infection, or behavior of 22 children aged one to two years, as compared to 25 controls receiving a placebo.

D. A. Craigmile, J. E. Preston, and W. T. C. Berry. *Month. Bull. Min. Health* 15: 78, 1956.

DRIED blood from butchered animals or animal donors is said to be a valuable source of proteins, especially the amino acids histidine and tryptophan. Incorporated into recipes used in Russian clinics and hospitals, it has been found to constitute a useful means of increasing the protein content of therapeutic diets.

A. E. Sharenak, A. S. Arefyeva, and B. S. Kariysheva. *Voprosy Pitaniya* 15: 22, 1956.

BLOOD SUGAR did not rise rapidly when sugar was ingested together with protein (calcium caseinate) or fat (butter). Delayed gastric emptying or competitive absorption may be responsible.

J. H. Fryer. *Fed. Proc.* 15: 552, 1956.

A STANDARD parenteral load of vitamin B_{12} was administered to normal subjects and to patients suffering from acute and chronic diarrhea. The amount of vitamin B_{12} excreted with the urine during the 24-hour period following the load was lower in diarrheal subjects than in normal ones, thus showing the body's tendency to retain the vitamin. This means that in diarrheal subjects, even when no hematologic alterations occur, there is a deficiency state of vitamin B_{12}, which is also shown by the cobalamine levels in the serum.

G. Allegra and R. Niutta. *Acta Vitaminol.* 2: 71, 1956.

EDEMATOUS patients with heart disease were found to have a higher ratio of body sodium to body water in their bodies than edematous patients with hepatic or renal disease.

S. J. Farber and R. J. Soberman, *J. Clin. Investigation* 35: 779, 1956.

RECENT ADVANCES IN EXPERIMENTAL NUTRITION

DIETARY FAT is effective in reducing protein catabolism. Recent studies indicate that stress conditions increase the need for highly unsaturated fatty acids.

H. M. Fox, P. P. Swanson, and E. Birds. *Fed. Proc.* 15: 551, 1956.

ACCORDING to recent studies digestibility of fats is dependent upon the chain length of the saturated fatty acids and their arrangement within the glyceride structure.

D. H. Calloway and G. W. Kurtz. *Fed. Proc.* 15: 545, 1956.

A PURIFIED pantothenic acid-deficient diet led to fetal death in as high as 63 per cent of pregnancies, and development of congenital abnormalities in as much as 23 per cent of living young rats.

H. M. Evans, M. M. Nelson, C. D. C. Baird, and H. V. Wright. *Fed. Proc.* 15: 549, 1956.

THE "ANTIVITAMIN," pyrithiamine, lowers the thiamine content in nerve tissue (brain) by an unknown mechanism. Oxythiamine, another antagonist, has no significant neurologic effect

L. De Caro, G. Rindi, V. Perri and G. Ferrari. *Experientia* 12: 300, 1956.

VITAMIN E deficiency in monkeys is characterized by a specific anemia. A reticulocyte response can be elicited by administration of α-tocopherol.

P. L. Day and J. S. Dinning. *Fed. Proc.* 15: 548, 1956.

THE SAME amounts of the essential amino acids were found to be present in both crude casein and casein without animal protein factor. Animal protein factor deficiency would thus seem to be due to a deficiency of factors present as impurities in crude casein, rather than to a lack of any of the essential amino acids.

M. Marchetti, R. Viviani, and A. Rabbi. *Intern. Ztschr. f. Vitaminforsch.* 26: 339, 1956.

Nutritional Quotes

Heart Disease in Young

"An investigation of the incidence of arteriosclerotic heart disease in the younger age group of a large necropsy population over the last 34 years discloses that the total arteriosclerotic heart disease frequency has not changed. However, there is an increase in its occurrence in the younger age group, the most striking increase in frequency occurring between the ages of 40 to 50. During the same period of time the necropsy population has become increasingly older. Since arteriosclerotic heart disease among the total necropsy population has not changed appreciably, factors other than diet may be responsible for this increase in arteriosclerotic heart disease among the younger age group."
—O. Saphir, L. Ohringer, and H. Silverstone. *Am. J. Med. Sc.* 231: 494, 1956.

Post-operative Intake of Protein Important

"Whether we consider the tissue or the blood proteins in patients following operation, severe injury, or even severe non-surgical disease, the best results will follow if early attention is given to the intake of protein and, of course, other food essentials. By applying present knowledge and techniques and by discussing fully with the dietitian the various clinical problems, severe and cumulative protein deficiencies should no longer increase the risk of operation and the complications after operation, but should materially aid in leading to the safest and the most rapid restoration of the surgical patient to complete health."
—R. Elman. *J. Am. Diet. A.* 32: 526, 1956.

Something to Chew On

"The purpose of our teeth is a physical and not a chemical one. Having lost their motive for existence, our teeth are taking a course leading us fast toward becoming homo edentatus plasticatus; it is doubtful whether we can forestall this fate with chemical maneuvers.

"Today we know of the extensive, all-pervading network of the organic enamel matrix with its metabolic potentialities; we are aware of the potent variable of pressure in biology and in physics, and we know what lack of loads does to the structure of the femur, particularly of the immobilized child. As the tooth in all its strata is no longer considered inert, it must be recognized that either lack of loads with our soft foods or higher compression cannot fail to influence its structure throughout.

"Instead of the frustrating insistence on narrow dietary regimes, attempt unpackaged, hard-crusted bread, as the ends of rye or corn bread, pumpernickel or Italian bread at the earliest age. Our trend to strained, chopped baby foods, euphemistically termed solids, inculcates an aversion to chewing. Parents should realize that their infants will not choke on less cooked and harder foods, and that the tooth structure will greatly benefit thereby.

"Our teeth need a heavier load—in addition to our customary soft diet. This aim can be achieved."
—H. H. Neumann (Letter). *J. Am. Dental A.* 52: 757, 1956.

Measuring Cellular Potassium Status

"Total body exchangeable potassium is approximately 40 mEq./kg. of body weight in infants, children and young adults alike, in contrast to exchangeable water and sodium which are high per unit of body weight at birth and decrease to adult levels during the first 2 years of life.

" 'Cell potassium concentration' calculated from exchangeable water, sodium and potassium and serum sodium concentration changes little during the period of growth and development despite other large alterations in body composition.

"These measurements are suggested as a further means of investigating cellular potassium status *in vivo*."
—L. Corsa, Jr., D. Gribitz, C. D. Cook, and N. B. Talbot. *Pediatrics* 17: 189, 1956.

Protein and Hepatic Coma

"The relationship between ammonia intoxication and impending hepatic coma, and even deep coma, produced by protein and other nitrogenous substances such as ammonium chloride, is by no means clear. It is true that some patients have a high venous blood level of ammonia when hepatic coma develops, but the relation is not yet distinct nor constant enough to imply an etiological relationship. The empirical fact remains that, in certain patients, hepatic coma may be induced by protein, whatever the biochemical defect may be."
—C. S. Davidson. *J.A.M.A.* 160: 391, 1956.

Reviews of Recent Books

Calcium and Phosphorus Metabolism. Ann. N. Y. Acad. Sc. 64: 279–462, 1956, $4.00.

Under the chairmanship of Franklin C. McLean, a two-day symposium was held at the New York Academy of Science, January 1956, on "Calcium and Phosphorus Metabolism." The topics covered by active workers in their fields included calcium balance and turnover studies, parathyroid hormone, calcium complexing agents, parturient paresis in dairy cows and special aspects of calcium metabolism including rickets, vitamin D, and osteoporosis.

It is difficult to select any one of the 18 papers for special mention: all are of high quality and fully documented and illustrated. Nevertheless, attention may be called to the report on the suppression of urinary calcium by oral sodium phytate by Henneman, Carroll, and Albright. In addition, Comar showed by radiocalcium studies that the fetal bones avidly take up calcium which is rapidly transferred across the placenta. Forbes' clinical studies on idiopathic hypoparathyroidism in children is very well done. All in all this particular conference seems to have produced much interesting and valuable information. S. O. W.

Infant Metabolism, World Health Organization, The Macmillan Company, New York, 1956, pp. 435, $8.00.

This book is a verbatim report of an international seminar on "Infant Metabolism" held in Stockholm, Sweden, in the fall of 1950 under the auspices of the World Health Organization. Participants were noted research workers in the field of infant nutrition from the Scandinavian countries and a visiting team from the United States. In the latter group were S. Z. Levine and H. L. Barnett from New York; O. A. Bessey, Chicago; Genevieve Stearns, Iowa City; and F. W. Clements, Geneva, Switzerland.

The purpose of the seminar was to bring together a selected group of medical investigators to permit an exchange of scientific information on the current physiologic, biochemical, nutritional, and clinical problems in infant metabolism. Each of the ten chapters represents a panel discussion on some specific topic. Included are panels on Water and Electrolyte Metabolism; Calcium, Phosphorous and Vitamin D; Protein Metabolism; Vitamins; Basal Metabolism; Metal Metabolism; Isotopes in Metabolism; Evaluation of Nutritive Status; Metabolism in Premature Infants; and Metabolism in Newborn Infants. Each topic is introduced by a formal presentation and followed by a general discussion.

Essentially the book is a review of the research work upon which many of the current practices in infant nutrition are based. Much of the material presented has been published previously, but in widely scattered medical journals. The comments, questions and discussions appear here for the first time. The reviewer found the different views expressed most intriguing and most informative.

The authors are to be congratulated upon bringing into one volume this wealth of material for the convenience of the interested reader. All pediatricians should find this a most valuable book and well worth reading from beginning to end.

One hesitates to include a criticism of any kind, but if one is justified, it would be that too long a time was permitted to elapse between the holding of the seminar (1950) and the publishing of the book (1956).

LEE FORREST HILL

Breads, White and Brown. Their Place in Thought and Social History, by R. A. McCance and E. M. Widdowson, J. P. Lippincott Co., Philadelphia, 1956, pp. 166, $5.00.

The authors of this little essay are among the leading British nutritionists. (The senior author is an editor for this JOURNAL.) They have managed to encompass in a small volume a highly documented (720 references) account of bread, not only as a nutrient, but as a matter of wide social and economic importance. From the days of Greece and Rome to the recent Wuppertal experiments (in which the authors played leading roles), bread seems to have had a unique position in the social and economic life of the population.

The controversy of brown versus white, of enriched versus unenriched breads seems to have had a long and complex history. White bread for centuries symbolized wealth, position, and perhaps "purity." Wholemeal bread symbolized the good old days, the simple life and perhaps rugged health. The perspective developed in this book should help dispel the emotional overtones in the evaluation of bread as a nutritious food. For as Seneca wrote two thousand years ago "If I am hungry I must eat. Nature does not care whether the bread is black or white: she does not want the stomach entertained but filled." S. O. W.

Amino Acid Handbook. Methods and Results of Protein Analysis, by Richard J. Block with the cooperation of Kathryn W. Weiss and several contributors. Charles C Thomas, Springfield, Ill., 1956, pp. 355, $10.50.

Dr. Richard J. Block who is the author with Diana Bolling of the well-known book *The Amino Acid Composition of Proteins and Foods* and of a recent monograph with Durrum and Zweig on Paper Chromatography, has incorporated in the *Amino Acid Handbook* in detail tried and proved examples of the most widely used methods of amino acid analysis, i.e., by micro-organisms, by column chromatography, by paper chromatography, as well as by chemical methods. The details of the methods are so clearly outlined that the reader has no need for recourse to the original literature. This handbook also has a complete bibliography and a comprehensive tabulation of the amino acid composition of proteins, biologically active polypeptides and foods. A novel feature of this publication is the amino acid content of hormones and bacteria, in indigenous foods and diets in different parts of the world, and in blood in various diseases. This book should prove invaluable to the investigator, biochemist, nutritionist, medical technologist, physician, dietitian and to all students of biochemistry and nutrition.

B. SURE

Ciba Foundation Symposium: Paper Electrophoresis, edited by G. E. W. Wolstenholme and E. C. P. Millar, Little, Brown and Company, Boston, 1956, pp. 224, $6.75.

The relatively recent development of practical chromatographic technics has had a tremendous effect in accelerating the progress of modern biochemistry. The even more recent use of paper electrophoresis as a clinical tool bids well to revolutionize many of our laboratory procedures. Only time will tell how far this trend will go, but some idea of the usefulness and limitations of paper electrophoresis is provided by the contributors to this useful book. This volume contains the proceedings of the symposium held in London, July 27–29, 1955, and includes detailed comments by many of the leading authorities in the field. Through formal papers and informal discussions, the application of paper electrophoresis to protein chemistry is quantitatively explored in the hope of standardizing methods, results, and apparatus. Among the many topics covered are evaluations of albumin-globulin ratios of blood, analyses of hemoglobins, lipoproteins, and the physico-chemical aspects of paper electrophoresis. This volume should be most helpful to anyone engaged in the study or practical application of electrophoresis methods.

M. K. HORWITT

Vitamins and Hormones. Advances in Research and Applications, Volume XIV, edited by R. S. Harris, G. F. Marrian, and K. V. Thimánn, Academic Press, New York, 1956, pp. 432, $10.00.

Scientists look forward to the publication of the annual edition of Vitamins and Hormones. The fourteenth volume maintains the standards of excellence set by the previous collections of reviews. Eight topics are covered. Those specifically nutritional are Mickelsen's survey of intestinal synthesis of vitamins and Lowe and Morton (Liverpool) on vitamin A metabolism. But special mention must also be made of the fine review of carbohydrate metabolism in isolated tissues by Renold Ashmore and Hastings, and of experimental hyperglycemias by Shull and Mayer. The many references and the detailed author and subject indexes add to the usefulness of the book.

Nutrition is a subject that crosses all clinical lines and is closely related to practically every branch of biology. It is fortunate, indeed, that there exist several excellent sources of integrated surveys, such as this book, for they are essential for future investigational work. The editors and authors are to be complimented for an excellent product.

S. O. W.

The Complete Book of Low Calorie Cooking, by Leonard Louis Levinson, with introduction by Leonid Kotkin, M.D., Hawthorn Books, Inc., New York, 1956, pp. 319, $4.95.

There is indeed no shortage of books for the individual who wishes to lose weight, and the choice of a reliable guide is not easy for the uninformed. The author, a writer of radio and television scripts, short stories, and another cookbook, has consulted many physicians, dietitians, and home economists in the preparation of the book.

The purpose of this book is "to supplement the doctor's general instructions and to help you carry out his orders." Accordingly, the greater part is devoted to some 600 recipes for all kinds of foods.

The recipes, as a rule, are of family size and are sufficiently interesting to be acceptable by non-dieters as well. Caloric values for single portions are indicated. Within a food group there is a fairly wide range of caloric levels. With a nutritionally adequate diet pattern, it would be possible to use these recipes to plan widely varied menus at any one of several caloric levels as might be prescribed by the physician.

For the most part, the ingredients are those readily available, methods of preparation are clearly detailed, and time of preparation need not be great. Many recipes using artificial sweeteners are included.

An introductory chapter is concerned with desirable body weights, the importance of proper nutrition and the use of the Basic Seven food groups, and some concise "Do's and Don'ts" by past and present celebrities in various walks of life. The information on the whole appears to be correct, although the statement concerning the need for carbohydrate "because fat will not be consumed by the body unless there is carbohydrate to make it burn properly" (page 21) is no longer tenable. The caloric recommendations are those of the 1948 Recommended Dietary Allowances, and not the 1953 revision.

The list of artificial sweeteners, 50 sensible snack foods, a summary of spices, herbs and their uses, and a listing of some 800 dietetic foods should provide useful helps to many dieters. On the other hand, this reviewer questions whether space need be given to listing numerous appliances such as blenders, mixers, grinders, cook-

ing pans, etc. Certainly the success of a low calorie diet is not dependent upon gadgetry!

This book will have appeal to those dieters who have been unsuccessful in achieving variety and palatability, and it emphasizes once again that a low calorie diet need be neither difficult to prepare nor lacking in appeal.

C. ROBINSON

The Use of Chemical Additives in Food Processing. A Report by the Food Protection Committee of the Foods and Nutrition Board, National Academy of Sciences, National Research Council, Publication 398, 1956, pp. 90, $2.00.

Intentional chemical additives have been defined by the Food Protection Committee of the National Research Council as those chemicals introduced for the purpose of imparting some desired quality to, or of serving a functional purpose in, a food product. Such materials as coloring agents, flavors, vitamins and minerals for food fortification, non-nutritive sweeteners, preservatives, antioxidants, emulsifiers, and bleaches are all *intentional additives*.

A survey of the food and chemical industries has been conducted by the Food Protection Committee to ascertain the identity and qualities of intentional additives used in food processing. In addition to the replies from the food and chemical industries, the definitions and standards for processed foods published by the Food and Drug Administration and the regulations for meat products and fats published by the Meat Inspection Branch of the Department of Agriculture have been used as source material.

The resulting lists incorporated in this publication represent the most complete available tabulation of additives used in processed foods. It is recognized that these lists are subject to several limitations: (1) they may contain additives permitted by regulations but not in actual use; (2) an additive may be used seasonally or by some segments of an industry but not by others; (3) amounts given may represent maximum usage rather than actual usage and thus not permit reliable quantitative estimation of consumption; (4) each class of additives represents a group of alternative ingredients from which a selection may be made for use in a particular product. It is the intention of the Food Protection Committee to revise these lists as new information warrants.

B. SURE

Internal Secretions of the Pancreas. Ciba Foundation Colloquia on Endocrinology. Vol. 9. Little, Brown & Company, Boston, 1956, pp. 287, $7.00.

This book presents some 17 reports made at a symposium on the endocrine aspects of the pancreas held in London in 1955 under the aegis of the Ciba Foundation. A wide range of topics is covered by a group of internationally recognized experts. Because they represent diverse disciplines—biologists, clinicians, and physical, biologic, and organic chemists—their different viewpoints are refreshing and stimulating. That many problems remain unsettled is, however, to be expected. Perhaps most interesting of all are the verbatim reports of the give-and-take discussions held after formal presentation of the papers.

The topics discussed are based on the actions and chemical characteristics of both glucagon and insulin. This field is under intensive investigation and therefore more questions are raised than answered. Because of the implications of this aspect of carbohydrate metabolism for clinical nutrition, the book will be of interest to all concerned with the triplets—nutrition, metabolism, and endocrinology.

S. O. W.

Ciba Foundation Symposium on Bone Structure and Metabolism, edited by G. E. W. Wolstenholme and C. M. O'Connor, Little, Brown and Company, Boston, 1956, pp. 299, $8.00.

This volume represents the proceedings of an informal international get-together of workers interested in bone morphology and physiology. Such discussions are arranged in order to stress integration of views rather than presentation of new findings by the participants. Even though an undertaking of this kind has necessarily to be limited in scope, the book will serve as a useful and stimulating guide to the student and physician interested in the subject matter, and as a source of quick reference for those already familiar with the problems discussed.

Of the total of 20 papers eleven are devoted to basic aspects of formation and resorption of the mineralized tissues and their ground substance. The processes involved are reviewed and discussed from the morphologic, biochemical, and chemical angle with consideration of the results obtained by radio-autography, phase microscopy, electronmicroscopy, determination of the turnover of P^{32} and S^{35}, and the uptake and exchange of bone citrate. Only some highlights will be mentioned here.

Vitamin D metabolism and its systemic distribution as indicated by paper chromatography of tissue extracts and by studies with C^{14} are discussed by Kodicek, and the mode of action of vitamin D by Nicolaysen and Eeg-Larsen. Fanconi reports on variations in the sensitivity to vitamin D. A series of clinical disorders associated with varying degrees of sensitiveness are recognized ranging from vitamin D-resistant rickets to chronic hypercalcemia. The hypothesis is advanced that in most, if not in all, types of rickets renal function, particularly of the tubules, is impaired as indicated by the association of rickets with hypochloremic acidosis, hypercalcemia, and aminoaciduria. The disposition to rickets would thus consist in the disposition to tubular insufficiency. Clinically, reduced sensitivity to vitamin D would be indicated by familial disposition to rickets and to aminoaciduria, while such conditions as hypothyroidism, retarded growth and x-ray signs of hypercalcification of the provisional cartilage point to increased sensitivity. This theory certainly needs further substantiation before it can be accepted.

Blaxter demonstrated that in cattle, sheep, and horses

suffering from hypomagnesia as indicated by lactating tetany, Mg is removed from all parts of the skeleton, while calcium is retained in slightly increased amounts. Calcification of the cartilage however is not disturbed. The serum level of inorganic P is unaffected, and phosphatase activity at the site of mineralization seems to be normal. Magnesium is probably concentrated by osteoblasts, and depletion takes place by removal of Mg from the surface of the bone crystal. Bones of old animals seem to be more resistant to depletion than those of young animals.

Follis reports that in rats cessation of growth was induced by underfeeding. Subsequent treatment with growth hormone in amounts larger than necessary to promote growth in hypophysectomized rats failed to be effective in the underfed animals. This seems to indicate that the effect of underfeeding is not mediated through a hypoactive pituitary. The bone changes in lathyrism which are due to the presence of β-aminopropionitrile in the diet are discussed. The effect of copper deficiency appearing in the long bones of animals grazing in Cu-deficient areas consists of thinning of the bones probably due to decreased osteoblastic activity. In the bones of rats, hypervitaminosis D manifests itself in formation of osteoid that fails to calcify in spite of the coexisting hypercalcemia and hyperphosphatemia.

A new syndrome in infants, osteodysmetamorphosis foetalis, is defined by Engfeldt and Zetterström. It is characterized by low serum and tissue alkaline phosphatase activity. In this type of hypophosphatasia, skeletal development is inhibited, bone formation decreased, and mineralization of the newly formed matrix is deficient. The coexistent hypercalcemia is considered secondary to increased calcium absorption from the gastrointestinal tract, and the nephrocalcinosis observed in some cases secondary to hypercalcemia. The parathyroids do not show morphologic changes. The cause of the syndrome is unknown, and may be under genetic control.

The clinical nutritionist will find the case studies and some of the experimental findings of interest. The discussions permit the reader a better evaluation of the data presented and of the views expressed by the various participants.

M. SILBERBERG

Books received for review by THE AMERICAN JOURNAL OF CLINICAL NUTRITION are acknowledged in this column. As far as practicable those of special interest are selected, as space permits, for a more extensive review.

Handbook of Biological Data, edited by William S. Spector, W. B. Saunders Co., Philadelphia, 1956, pp. 584, $7.50.

The Physician-Writer's Book by Richard M. Hewitt, W. B. Saunders Co., Philadelphia, 1956, pp. 415, $9.00.

Experimental Methods for the Evaluation of Drugs in Various Disease States, edited by O. V. St. Whitelock and F. N. Furness, Annals N. Y. Academy of Sciences, 1956, pp. 462, $4.00.

Biochemical Individuality by Roger J. Williams, John Wiley & Sons, Inc., New York, 1956, pp. 214, $5.75.

The Biological Basis of Human Freedom by Theodosius Dobzhansky, Columbia University Press, New York, 1956, pp. 135, $2.95.

Communication by Roy Ivan Johnson, Marie Schalekamp, Lloyd A. Garrison, McGraw-Hill Book Co., New York, 1956, pp. 361, $4.50.

Cortico-Surrenale et Diabete Humain by B. Bastenie, Masson et C^ie^, Paris, 1956, pp. 506, 3,400 fr. francs (paper bound), 4,000 fr. francs (cloth bound).

Experimental Design by Walter T. Federer, The MacMillan Co., New York, 1955, pp. 544, $11.00.

Soybeans for Health, Longevity and Economy by Philip S. Chen, The Chemical Elements, South Lancaster, Mass., 1956, pp. 238, $3.00.

Abstracts of Current Literature

CHARLES R. SHUMAN, M.D., EDITOR

MARGARET W. BATES, D.SC., *Toronto*
ELIAS COHEN, PH.D., *Buffalo*
STANLEY W. CONRAD, M.D., *Philadelphia*
A. B. EISENSTEIN, M.D., *St. Louis*
K. R. CRISPELL, M.D., *Charlottesville*
M. K. HORWITT, PH.D., *Elgin*
F. E. HYTTEN, M.B., B.S., PH.D., *Aberdeen, Scotland*
LAURANCE W. KINSELL, M.D., *Oakland*
S. M. LEVENSON, M.D., *Washington*
STANLEY H. LORBER, M.D., *Philadelphia*
JOHN F. MUELLER, M.D., *Cincinnati*
MORTON J. OPPENHEIMER, M.D., *Philadelphia*
THEODORE C. PANOS, M.D., *Galveston*
JAMES H. SHAW, PH.D., *Boston*
MARTIN SILBERBERG, M.D., *St. Louis*
JANICE M. SMITH, PH.D., *Urbana*
JEREMIAH STAMLER, M.D., *Chicago*
BARNETT SURE, PH.D., *Fayetteville*
JOHN WATERLOW, M.D., *Kingston, Jamaica*

VITAMIN B_{12} AND ANEMIA

Much of the vitamin B_{12} in food is found in the form of a protein-cobalamine complex from which it is released by proteolytic enzymes and by heat. It is found almost exclusively in foods of animal origin and may be synthesized by micro-organisms in the rumen of animals. While the usual cause for deficiency states involving vitamin B_{12} is lack of intrinsic factor necessary for its transmucosal passage into the blood stream, occasional patients are encountered who do not consume the food sources of the vitamin. One group of persons known as "vegans" have been studied who consume a diet consisting wholly of vegetable products. This type of diet has led to combined degeneration of the spinal cord. It is of interest that aureomycin administration improved the subnormal vitamin B_{12} blood levels of vegetarians.

Pernicious Anemia Due to Dietary Deficiency of Vitamin B_{12}. M. Pollycove, L. Apt and M. J. Colbert. *New England J. Med.* 255: 164, 1956.

Pernicious anemia develops due to a deficiency of vitamin B_{12} and is usually ascribed to the inability of an organism to absorb the vitamin because of lack of an intrinsic factor present in gastric juice. This paper describes a case of pernicious anemia in which there was an actual lack of dietary vitamin B_{12}. The patient described had avoided all foods of animal origin for at least eight years.

Clinical tests showed the classic morphologic changes of blood and bone marrow found in pernicious anemia except for leukopenia. After administration of vitamin B_{12} there was an increase in red blood cell and platelet counts. The level of serum vitamin B_{12} before therapy was in the range found in cases of pernicious anemia. The serum iron content before therapy was low but increased during the 30 days following vitamin B_{12} therapy, then decreased. The latent iron-binding capacity acted in a reverse manner, decreasing during the first 30 days of treatment, then increasing. The authors ascribed these changes to variations in rates at which plasma iron was being utilized by the bone marrow for erythropoiesis. The absorption of vitamin B_{12}, as shown be fecal elimination and hepatic deposition of cobalt^{60}-labeled vitamin B_{12}, were normal on the twenty-fifth day of treatment. Urinary excretion of the labeled vitamin B_{12} was in the normal range on the fifty-third day.

As far as the authors know this is the first documented case of pernicious anemia resulting from a dietary insufficiency of vitamin B_{12}—M. W. BATES

Vitamin B_{12} Deficiency Due to Defective Diet. R. J. Harrison, C. C. Booth, and D. L. Mollin. *Lancet* 1: 727, 1956.

Megaloblastic anemia due to inadequate dietary intake of vitamin B_{12} is extremely rare in temperate zones.

A case is described of a 77-year-old woman who had a gastroenterostomy in 1919 for duodenal ulcer and who since 1943 had existed on a diet of bread and margarine, potatoes, and tea. Her only source of animal protein was a little milk in tea. She was in extremely poor condition, her hemoglobin was 5.4 g/100 ml, packed cell volume, 18 per cent, and mean corpuscular volume 150 cμ. Her sternal marrow showed severe megaloblastic changes and her serum vitamin B_{12} level was 75 $\mu\mu$ g per ml. She was achlorhydric and had an atrophic gastritis, demonstrated by biopsy. The fat balance was normal. Absorption of radioactive vitamin B_{12} was normal.

Treatment with vitamin B_{12} and iron effected a

dramatic improvement in both the anemia and in her condition generally.—F. E. HYTTEN

Anemia and Vitamin B_{12} Dietary Deficiency. F. Wokes. *Proc. Brit. Nutrition Soc.* 15: 134, 1956.

Dietary deficiency of vitamin B_{12} with low serum levels occurred in persons termed "vegans" after several years on a diet containing no animal food. This deficiency did not lead to the characteristic blood picture of pernicious anemia, or indeed to any pronounced macrocytosis, but it was accompanied by marked changes in the nervous system, extending in some instances as far as subacute combined degeneration of the cord. An hypothesis is advanced to explain why the neurologic manifestations of pernicious anemia can be corrected by vitamin B_{12} but not by folic acid, which may apply to the "vegans" in whom these manifestations occurred. Lack of vitamin B_{12} would not only inhibit methionine synthesis but might also by inhibition of a sulfhydryl system lead to abnormal metabolism of tryptophan and tyrosine, with accumulation of toxic products. The author refers to alterations in sulphur metabolism in vitamin B_{12} deficiency being effected by large oral doses of tyrosine. Such doses have been found to produce a transient increase in the urinary excretion of thiocyanates in "vegans" with vitamin B_{12} deficiency.—B. SURE

The Effect of Vegetarianism and Antibiotics upon Proteins and Vitamin B_{12} in the Blood. G. A. Dhopeshwarkar, J. C. Trivedi, B. S. Kulkarni, R. S. Satoskar, and R. A. Lewis. *Brit. J. Nutrition* 10: 105, 1956.

In a previous study of the plasma-protein pattern of a hundred normal Indian students, the authors pointed out that there was an abnormal variation in the level of albumin and a significant elevation of the globulin fraction. Furthermore, this rise in globulin was associated with a high intake of vegetable proteins. In subsequent studies it was shown that the administration of 50 mg daily of various antibiotics over a period of two months led to a considerable rise in the level of albumin and a concomitant fall in the level of globulin, particularly the γ fraction. Studies in children, where a proportionately smaller amount of antibiotic was given, also indicated that the administration of broad-spectrum antibiotics could lead to a rise in serum albumin and a fall in globulin, when the latter was higher than normal to start with. The present investigation was undertaken to determine if there is a difference in the blood vitamin B_{12} level in vegetarians and individuals on a mixed diet, and further to study the effect of small doses of antibiotics upon the blood vitamin B_{12} level and to correlate this effect with the changes in plasma proteins. Ten normal medical students, including five vegetarians and five nonvegetarians, volunteered for the study. The diets of the vegetarians included milk and milk products but no other food of animal origin, and the diets of the nonvegetarians included eggs and fish, fowl, or meat daily. The vegetarians were then given 50 mg aureomycin daily for two months, and the determinations were repeated after one and two months.

The albumin content of the plasma was below normal and the globulin content above normal in the vegetarian students, who also had a lower blood content of vitamin B_{12} than the nonvegetarians. The administration of aureomycin to the vegetarians produced a rise in plasma albumin and a fall in the globulin fractions. Values for blood vitamin B_{12} increased significantly.—B. SURE

The fish tapeworm infestation produces a type of megaloblastic anemia which responds to vitamin B_{12}. The low serum vitamin B_{12} levels is indicative of the diversion of the vitamin from the pathways of absorption in the host by the parasite.

Low Vitamin B_{12} Concentrations in Serum in Fish Tapeworm Anemia. W. Nyberg and G. Ostling. *Nature* 178: 934, 1956.

Megaloblastic anemia occurring in carriers of the fish tapeworm (*Diphyllobothrium latum*) presents a similar hematological picture to that of true pernicious anemia. It has been suggested that the worm deprives the host of vitamin B_{12}. Serum vitamin B_{12} levels were estimated in eight subjects with anemia associated with an infestation of worms and in 20 convalescent medical patients suffering from other conditions. The levels found in the controls ranged from 180 to 964 $\mu\mu$g vitamin B_{12}/ml. In those with tapeworm anemia, seven were below 50 and the eighth had a level of 65 $\mu\mu$g vitamin B_{12}/ml.—F. E. HYTTEN

The diagnosis of pernicious anemia in treated patients has presented a serious problem until recent years. The use of Co^{60} labeled vitamin B_{12} has obviated this difficulty by permitting measurement of the absorption of the vitamin. The three methods available for such determinations are the hepatic uptake, the fecal elimination, and the urinary excretion of the labeled vitamin administered orally.

Absorption, Elimination and Excretion of Orally Administered Vitamin B_{12} in Normal Subjects and in Patients with Pernicious Anemia. M. Pollycove and L. Apt. *New England J. Med.* 255: 207, 1956.

Vitamin B_{12} absorption was determined in patients with pernicious anemia and in normal subjects using three methods: fecal elimination, urinary excretion and hepatic deposition of the radioactive (cobalt^{60}-labeled) vitamin B_{12}. Feces were collected for 10 days after the ingestion of the radioactive vitamin B_{12}. Total counts obtained from the feces were compared to the total count of the vitamin ingested. This was expressed as the percentage of the ingested radioactive vitamin B_{12} eliminated in the feces. To measure vitamin B_{12} excretion in the urine, a large subcutaneous "flushing" dose of unlabeled vitamin B_{12} was administered at the

same time as the radioactive vitamin B_{12} was ingested. Counts were obtained from urine collected during the next 24 hours. The hepatic deposition of the vitamin was determined 10 days after the feeding of the radioactive vitamin by placing the crystal of a mobile scintillation counter-head on the body surface over the liver.

The results obtained using the three methods were relatively consistent. Fecal elimination and hepatic deposition of the radioactive vitamin B_{12} showed that absorption of the vitamin ranges from 62 to 82 per cent in normal subjects and 5 to 15 per cent in patients with pernicious anemia. Normal subjects excreted 7.3 to 10.3 per cent of the ingested vitamin B_{12} in the urine; patients with pernicious anemia, 0.6 to 1.0 per cent.

The authors found the measurement of hepatic deposition of the radioactive vitamin B_{12} the best method as far as simplicity, ease and accuracy was concerned. The chief disadvantage was that several days had to elapse after the feeding of the radioactive vitamin B_{12} before a measurement could be made. The fecal elimination method, while a direct method, has the disadvantage that feces have to be collected for 10 days after the radioactive-vitamin B_{12} feeding to insure that most of the labeled-vitamin B_{12} has been excreted. Since it is important that all the feces be collected it is necessary to have complete cooperation from the subject. The urinary excretion method is unsuited for measuring the percentage of vitamin B_{12} absorbed and requires a massive subcutaneous "flushing" dose of unlabeled vitamin B_{12} that may act as a therapy prematurely in certain cases of pernicious anemia.—M. W. BATES

An Improved Urinary Excretion Test as an Assay of Intrinsic Factor. III. Comparison of Results of this Method with the Classical Clinical Method. W. L. Williams, L. Ellenbogen, S. F. Rabiner, and H. C. Lichtman. *J. Lab. & Clin. Med.* 48: 511, 1956.

The measurement of the amount of radioactivity present in the urine of a subject subsequent to the ingestion of Co^{60}-labeled Vitamin B_{12} has proven a valuable aid in the diagnosis of pernicious anemia. It can also be used to assay the efficacy of materials possessing intrinsic factor activity. This paper is further documentation of this usefulness. Twenty-two such materials were so tested and the results compared to the classic clinical test which is so time-consuming. It was found that those intrinsic factor substances which produced a positive urinary excretion test also were potent when tested clinically, although the reverse was not always true. It would appear, therefore, that the urinary excretion test is a safe method for evaluating the potency of intrinsic factor materials because whatever error there may be, is on the right side.

However, the known variability of response in a given patient to the oral administration of Vitamin B_{12} and intrinsic factor would seem to the abstracter to make imperative the performance of an urinary excretion test on each patient with pernicious anemia so treated. If this is impractical, then the intramuscular injection of Vitamin B_{12} remains the most economical and safe method of treating pernicious anemia.—J. F. MUELLER

The pathogenesis of megaloblastic anemias may be determined by simultaneous administration of intrinsic factor with Co^{44}-labeled vitamin B_{12}. If the absorption of the vitamin is not favored by intrinsic factor one may assume that the condition is not solely due to primary pernicious anemia.

The Absorption of Vitamin B_{12} in the Megaloblastic Anemias. J. R. Evans. *Proc. Brit. Nutrition Soc.* 15: 126, 1956.

Studies with labeled-vitamin B_{12} reveal distinctive patterns of absorption which may be useful in classifying the different forms of megaloblastic anemia according to their pathogenesis. When impaired absorption is due to lack of intrinsic factor, the defect may be corrected by giving small amounts of intrinsic factor together with the oral dose of labeled-vitamin B_{12}. Where anemia is associated with intestinal disease the absorption of labeled-vitamin B_{12} is rarely improved by the usual doses of intrinsic factor but may be increased by very large doses. In some patients with structural abnormalities of the intestine failure to absorb labeled-vitamin B_{12} is corrected by sterilization of the bowel suggesting that bacterial contamination of the small intestine is responsible for the interference with absorption. In other forms of megaloblastic anemia there appears to be no defect in the absorption of vitamin B_{12}—B. SURE

The usual macrocytic anemia of pregnancy has been found to be responsive to folic acid therapy rather than to vitamin B_{12}. The latter agent has not been effective in most previous reports.

Treatment of Megaloblastic Anemia of Pregnancy and the Puerperium with Vitamin B_{12}. E. B. Adams. *Brit. Med. J.* 2: 398, 1956.

The effect of treatment with vitamin B_{12} is described in 10 subjects with megaloblastic anemia associated with pregnancy. Two were Africans and eight Indians. Their diets were thought to be inadequate. Before treatment their hemoglobin levels ranged from 3.1 to 6.9 g/100 ml and the mean cell volume ranged from 89 to 144 $c\mu$. All 10 subjects had the diagnosis confirmed by bone marrow biopsy; metamyelocytes were present in all, six showed megaloblasts and the other four cells of intermediate type.

In seven cases treated in the puerperium, 100 mg of vitamin B_{12} daily for one to fourteen days gave a good response. In the other three subjects, who were treated during pregnancy, two showed no response and one was inconclusive. It is suggested in the discussion that there may be several varieties of megaloblastic anemia associated with pregnancy.—F. E. HYTTEN

Vitamin B_{12} has been shown to exert a powerful effect upon reduction systems and has been implicated in the formation and in the reactions involving single methyl groups.

Vitamin B_{12} and Protein Metabolism. K. M. Henry and S. K. Kon. *Brit. J. Nutrition* 10: 39, 1956.

In the last few years several papers have linked vitamin B_{12} with the metabolism of proteins in different animals. The authors have studied the effect of vitamin B_{12} on protein metabolism in a series of experiments with vitamin B_{12}-deficient and normal rats. For deficient rats the biologic value of casein was increased to the same extent by the addition of 1 per cent methionine as by the addition of 1 per cent homocysteine and a vitamin B_{12} supplement. Homocysteine was ineffective in the absence of the vitamin. It is concluded that vitamin B_{12} functions in the synthesis of methyl groups. With deficient rats the addition of 1 per cent homocysteine, together with 0.5 per cent choline, in the presence or absence of vitamin B_{12}, increased the biologic value of casein to the same extent as 1 per cent methionine. This finding demonstrates that the vitamin plays no part in transmethylation. With normal rats vitamin B_{12} did not increase the biologic value of soya or of casein at a high (16 per cent) level of protein intake. It is concluded that vitamin B_{12} plays a part in the synthesis of methyl groups but that it neither functions in transmethylation nor is involved in protein utilization as such.—B. SURE

Effect of Orotic Acid on Vitamin B_{12}-Deficient Rats. M. Marchetti, R. Viviani, and A. Rabbi. *Nature* 178: 805, 1956.

Three groups of weanling rats were fed on the following three diets: (1) a basal vitamin B_{12}-deficient corn soy-bean meal diet, (2) basal diet supplemented with 2 γ vitamin B_{12} and (3) basal diet supplemented with 1000 k orotic acid/100 g.

Judged in terms of growth rate and the activity of liver betaine-homocysteine transmethylase, both of which are reduced in vitamin B_{12} deficiency, the rats did almost equally well on both diet (2) and diet (3). These data suggest a metabolic relationship between orotic acid and vitamin B_{12}.—F. E. HYTTEN

The Effect of Vitamin B_{12} on the Red Cell Size in Pernicious Anemia. J. F. Adams. *Scot. Med. J.* 1: 227, 1956.

Although there is unanimous agreement that vitamin B_{12} is curative in pernicious anemia, several recent studies have reported that the macrocytosis may persist after clinical cure, suggesting that vitamin B_{12} is not entirely adequate.

The blood of 17 patients with pernicious anemia, treated by vitamin B_{12} alone and in therapeutic remission was studied and compared with blood from normal control subjects. The mean cell volume, mean cell diameter and mean cell average thickness were entirely normal in the treated anemia group.—F. E. HYTTEN

FAT EMULSIONS FOR PARENTERAL AND ORAL USE

The need for a substantial increase in the caloric value of parenteral nutritional programs could be met readily by the incorporation of fatty acids in the intravenous fluids. Many investigators have sought to prepare suitable emulsions of fats for parenteral use; however, the occurrence of side-effects in a substantial number of patients receiving these preparations has prevented their general acceptance. In those patients receiving fat emulsions without undesirable reactions, the increased energy intake has resulted in a definite nitrogen-sparing effect.

Metabolic Effects of Fat Emulsions Administered Intravenously to Human Subjects. W. B. A. Bentley and T. B. Van Itallie. *J. Lab. & Clin. Med.* 48: 184, 1956.

Studies on the metabolic effects of a 15 per cent fat emulsion administered intravenously to four healthy volunteers maintained on constant diets, inadequate in calories and adequate in protein, are described.

The negative nitrogen and potassium balances produced by caloric deprivation were significantly decreased in three out of four subjects by the addition of extra calories as provided by the intravenous fat emulsion. Oral fats in amounts similar to the amounts supplied by the intravenous emulsion were also effective.

Although the authors state that studies with intravenous fat preparations have been limited because of side effects, no mention is made of side effects in this study except that one subject developed diarrhea. The investigation also suffers from a lack of baseline before the subjects were placed on the low-calorie diet and the short periods that the studies were actually carried out. The results appear to be significant but would be more impressive if longer control and treatment periods had been used.—K. R. CRISPELL

A logical approach to the problem of finding a suitable preparation for intravenous fat feeding is that of utilizing the fatty acids. The evidence at hand suggests that the free fatty acids represent the readily oxidizable lipid forms. A glucose ester of fatty acids is described which may provide a satisfactory medium for administration of calories.

Parenteral Calories from a Synthetic Water Soluble Fat. H. H. Leveen. *Surg., Gynec. & Obst.* 102: 154, 1956.

The inadequacy of available carbohydrate solutions for the provision of adequate calories when nutritional requirements must be met solely by the parenteral route has been long recognized. The long infusion times, the large volumes, and the osmotic effects are some of the drawbacks of the various sugar solutions. The limitations of intravenous alcohol are also well known. Attempts to prepare a fat emulsion suitable

for intravenous use have met, so far, with limited success. That emulsified fat given intravenously can be metabolized has been demonstrated, but infusion of all preparations hitherto available has led to various undesirable reactions (fever, back pain, blood pressure and pulse changes) in a number of the recipients. The basis for these reactions has not been clarified, but it has been suggested that they may be related to the particulate character of the fat emulsions and/or to the emulsion stabilizers. With this in mind, Leveen reports the synthesis of a water-soluble molecule which theoretically should yield 6.2 cal/g about half-way between the caloric yields of carbohydrate and fat. This compound is a glucose ester of aleuritic acid.

Aleuritic acid is a naturally occurring 16-carbon fatty acid with hydroxyl groups on the ninth, tenth, and sixteenth carbon atoms. The author states that rat liver mitochondria metabolize this substance *in vitro* in a manner almost identical to palmitic acid. However, aleuritic acid is precipitated in serum as the calcium salt. Accordingly, a glucose ester of aleuritic acid (GMA) was made. Neither the details of the synthesis nor its reproducibility are given. It is stated that GMA is completely water-soluble, stable, can be autoclaved, and is not precipitated in serum. It has no surface-active properties and, therefore, should not hemolyze red blood cells. A 13 per cent solution of GMA is isotonic with 5 per cent glucose. One might conjecture, then, that a 26 per cent solution of the glucose monoaleuritate might be reasonably infused, providing, theoretically, about 1600 cal/lit.

Leveen presents a brief summary of data to be published in detail elsewhere (reference not given) suggesting the metabolic availability of glucose monoaleuritate given intravenously to a very small number of rats. He also mentions that animals receiving GMA had normal hemoglobin and red cell concentrations at the beginning and at the conclusion of the experiment. No data as to red cell survival or production are given. Autopsy and microscopic sections failed to reveal any abnormality in the animals receiving the GMA. It is to be hoped that the details of the metabolic and pathologic studies summarized in this paper will be reported soon.—S. M. LEVENSON

Infusion of fat emulsions may produce fever, backache, chills, urticaria, malaise and respiratory distress. The cause of these untoward reactions is not known. The rapid utilization of the infused lipids is indicated by the rate of clearing of the plasma and the absence of significant ketonemia.

Tolerance of Infants and Children to Fat Administered Intravenously with Particular Reference to Induced Ketonemia. M. L. Williams and R. Kaye. *A. M. A. Am. J. Dis. Child.* 90: 607, 1955, (Soc. Trans.)

The preparations (Lipomul, Upjohn) used in this study consist of 15 per cent of olive and cotton-seed oil in 4.2 per cent glucose solution, stabilized by soybean phosphatides and Pluronic F-68, and provide 1518 cal/lit.

One hundred-twenty-one infusions of approximately six hours' duration have been administered to 60 subjects between 13 days and 12 years of age, and 55 per cent of the experimental group under one year of age. The infusions provided approximately 50 cal/kg and were administered at an average rate of 5 ml/kg/hr (range, 1.5–9 cc).

Febrile reactions were encountered in 26 per cent of infusions, with elevations generally of the order of 2° F and of short duration. These reactions were in part related to infurion rate as shown by reduced incidence (13.6 per cent) in 66 infusions administered at rates below 5 ml/kg/hr. Four older children developed urticaria, in one instance associated with dyspnea and cyanosis which cleared completely in 30 minutes.

Thirteen infants under 21 months and two children six years of age received courses of four to six daily infusions, with all of the subjects exhibiting weight gains. Oral feedings were well tolerated during infusions. Blood chemical examinations were carried out before and after the course of infusions, with no change noted in serum nonprotein nitrogen, alkaline phosphatase, bilirubin, and cephalin-cholesterol flocculation. There was a single instance of moderate elevation of zinc turbidity. Routine urinalysis and urine urobilinogen values were likewise unchanged. In four infants there was a moderate drop in hemoglobin and red blood cell count, and in five infants a definite reticulocytosis was noted.

In 34 subjects changes in blood ketones at the end of six-hour fat infusions were determined. In subjects infused under nonfasting conditions blood ketones rose to an average value of 10.5 mg per 100 ml, expressed as acetone, while fasted subjects showed an average post-infusion level of 18.6 mg per 100 ml. The data indicate some utilization of fat during the period of infusion and provide evidence that the accumulation of blood ketones is not of sufficient magnitude to disturb the acid-base balance.

The rate of clearing of the infused fat was investigated in 16 experiments by serial determination of blood turbidity during and following the infusions. In more than half of the cases turbidity had fallen to control levels at three hours post-infusion, and in all except three instances at six hours.

The data suggest that with careful attention to rate of administration, calorically significant amounts of fat can be administered to infants without serious toxic effects. It appears at the present time that older children are less tolerance to the preparation used by the authors than are infants.—J. N. ETTELDORF

In the search for factors responsible for toxic reactions in the use of parenteral fat emulsions attention has been given to the role of the emulsifying agents employed in their preparation. Deterioration of these compounds on prolonged storage may limit their usefulness.

Decomposition of Lecithin in Parenteral Fat Emulsions. G. F. Lambert, J. P. Miller and D. V. Frost. *Am. J. Physiol.* 186: 397, 1956.

Aqueous solutions of alcohol-soluble phosphatide, synthetic lecithin and purified egg lecithin develop hemolytic and other toxic properties over a period of time at ordinary room temperature, or at an increased rate at 40° C. The toxicity of emulsions made with phosphatide as a stabilizer also increases with time. The evidence suggests tht hydrolysis of synthetic lecithin proceeds first to give a hemolytic product, presumably lysolecithin. When liberation of both fatty acids from L-alpha-dimyristoyl lecithin was complete and the myristic acid was removed, no toxicity was shown by the aqueous phase, presumably glyceryl phosphorylcholine. Attempts to decrease the hydrolysis of lecithin solutions did not suceed. Although the use of lecithin phosphatide preparations as emulsifiers for intravenous fat may have limitations as to time and temperature of storage, there is no clear indication from these studies that any real hazard is involved from the standpoint of clinical use.—AUTHORS

Oral fat emulsions of vegetable sources have been popularized in recent years. The need for such preparations in the usual hyperalimentation program is not convincing at the present time. For example, a nutritious high caloric tube feeding can be administered as pureed foods capable of maintaining body weight for long periods. For the purpose of raising the caloric value of the diet in undernutrition states for short periods, oral fat emulsions may prove useful. The influence of various dietary and other factors influencing absorption of fats supplied in this form requires further investigation.

General Nutritive Deficiency. R. M. Jamison. *Virginia Med. Monthly* 83: 67, 1956.

A stable oral fat emulsion was prepared which was said to be exceptionally well tolerated. It contained 6 cal/ml, was acid-stable, and did not deteriorate at room temperature. It was said to be readily miscible with liquids, milk, coffee, cola drinks, and fruit juices. At room temperature it was essentially odorless, and it was tasteless when administered in ice-cold chocolate milk.

Composed of refined vegetable (soybean) oil containing long-chain fatty acids, and sold under the name of "Nutramul," it was given to 28 patients of various ages and with various disorders. Weight gain was said to be at the rate of about 1 lb per lb of emulsion, although some patients gained 5–10 lb after one or two pints. Weight gain was enhanced by giving an "adequate" supply of B-complex vitamins.

There are insufficient data presented in this report to permit independent evaluation of the observations. Such statements as "the emulsion was administered to several patients with severe liver disease with an improvement in blood proteins, reduction of peripheral edema and reduction in liver size," are examples. Nevertheless, the subject is of obvious importance and perhaps more details will become available.—S. O. WAIFE

The Biological Value of Oils and Fats. H. J. Thomasson. *J. Nutrition* 59: 343, 1956.

Earlier experiments established that the increase in weight of young rats is dependent on the type of the dietary fat. These investigations further revealed that the different growth-action of the fats and oils investigated is actually due to a different food intake.

The rates of absorption of 18 natural oils and fats of vegetable and animal origin have been studied. It appears that these oils and fats could be divided into five groups according to a decreasing rate of absorption: (1) Butterfat; (2) Maize oil, cottonseed oil, beef tallow, coconut fat, soybean oil, sunflower oil, groundnut oil and olive oil; (3) Sesame oil, lard, palm fat and wheat oil; (4) Shea butter and herring oil; (5) Rapeseed oil, poppyseed oil and kapokseed oil. A significant correlation seems to exist between the rate of absorption and the growth-action of the oils and fats.

The fat recovered 3 to 11 hours after the administration of 400 mg per 100 cm^2 of body surface appeared to be distributed over stomach, small and large intestine, with a certain constancy, averaging 73, 22.5, and 5 per cent respectively.

The percentage of fat in the small intestine, seems to be independent of the absorption time and consequently of the amount of fat in the tract; that in the stomach showed a tendency to decrease, while that in the large intestine increased when absorption time was extended.—B. SURE

Effect of Choline, Methionine and Ethionine on Fat Absorption. H. C. Tidwell. *J. Nutrition* 58: 569, 1956.

The exact role of the phospholipids in the absorption of fat is uncertain at this time. A number of explanations have been suggested for the increased rate of fat absorption when lecithin or choline is ingested along with the lipid. In agreement with an earlier report, the rate of fat absorption was found by two methods to be accelerated when fat was supplemented with choline. The ability of the ingested choline to aid emulsification, as well as the failure of various hydrotropic substances to affect the rate of fat absorption, suggests that lecithin as well as choline is otherwise involved in the absorptive process.

The supplements of prostigmine and mecholyl used failed to affect the rate of fat absorption. This suggests that the effect of choline on the absorptive process cannot be that of a cholinergic one, but may be solely the result of an increased production of lecithin. The slight effect of a methionine supplement on the promotion of fat absorption might be the result of a failure to supply more physiologic amounts continuously, or of a synthetic process too slow to produce sufficient choline to be more effective.

The significantly increased blood-fat levels after the use of ethionine as a fat supplement might be associated with its reported liberation of a considerable amount of free methionine. This might well account for the accelerated rate of fat absorption, if the latter were continuously available in suitable quantities for additional choline and phospholipid formation which may in some way aid the passage of the fat into the intestinal mucosa.—B. SURE

IRON METABOLISM AND ANEMIA

Among nutritional disorders, that of iron deficiency anemia appears to be one of the most common throughout the world. Recent studies have demonstrated that a complex mechanism exists in the absorption and utilization of iron while protecting against an excessive accumulation of the element. The absorption of iron requires that it exists in the ferrous form. The mechanism of absorption involves transformation into apoferritin, a protein-iron complex, which may be partially converted to ferritin, the presence of which blocks further iron absorption. The conversion of iron to ferrous form is facilitated to a remarkable extent by the presence of ascorbic acid in the gastrointestinal tract. In iron-deficiency anemia, the uptake of labeled iron is enhanced, thus providing a diagnostic method in the evaluation of anemia. [An iron-tolerance test has been described in this JOURNAL *4: 609, 1956]*

Radioactive Iron Studies in Routine Haematological Practice. G. Wetherley-Mein, M. S. R. Hutt, W. A. Longmead, and M. J. Hill. *Brit. M. J.* 1: 1445, 1956.

The methods and materials are described for carrying out simple tests using injected Fe^{59}. These show the speed of clearance from the plasma, activity over various organs by surface counting, and the rate of red-cell utilization of the injected iron. Examples are given and the results discussed.

It is concluded that in practice the methods are simple and the hazards negligible, but "this technique is not an indispensable aid to diagnosis and treatment of the majority of patients with blood disorders."

It does, however, provide diagnostic short-cuts and is the only readily available laboratory technic by which the dynamics of erythropoiesis can be studied. It is "within the scope of any routine hospital laboratory which has haematologic responsibilities."—F. E. HYTTEN

A deficiency of iron may exist in patients with macrocytic anemia. This condition may be detected by noting hypochromia of the red blood cells, by determination of serum iron levels or by measurement of uptake of Fe^{59}.

Value of Serum Iron Levels in Assessing Effect of Haematinics in the Macrocytic Anemias. C. F. Hawkins. *Brit. M. J.* 1: 383, 1955.

High levels of serum iron occur in macrocytic anemias, falling during remissions and as a result of treatment. Estimation of the serum iron is a rapid means of assessing the value of treatment. In 23 cases of pernicious anemia, serial observations were made following a single injection of 100 μg of vitamin B_{12}. Twenty-one of the cases showed a significant fall in serum-iron level in 24 hours, and all in 48 hours. The "48-hour test" proved to be a reliable indication of the efficiency of treatment in 33 cases. An additional advantage of the serum-iron test was its indication of impending iron deficiency, shown by a fall to below 40 μg iron/100 ml plasma.—F. E. HYTTEN

The need for iron supplementation in pregnancy has been firmly established as re-emphasized in the following papers.

Administration of Iron in Antenatal Clinics. W. Edgar, and H. M. Rice. *Lancet* 1: 599, 1956.

A group of 179 pregnant women was divided into two series, one of which was given tablets of ferrous sulfate throughout pregnancy.

In the control group the hemoglobin level, red cell count, packed cell volume, and mean corpuscular hemoglobin concentration all fell (although the fall in M.C.H.C. is small and does not seem to have been tested statistically), whereas in the iron treatment group, all values were, on the average, maintained. Twenty of the latter group of 89 subjects did not "respond" to iron, in that their hemoglobin level fell. It is suggested that every expectant mother should receive iron as a routine measure.—F. E. HYTTEN

Iron Deficiency in Pregnancy. M. Fisher, and R. Biggs. *Brit. M. J.* 1: 385, 1955.

Women who are given iron by mouth during pregnancy almost always have a high hemoglobin concentration at term.

It is suggested that the response of the "physiological" anemia of pregnancy to iron indicates that it is due to iron deficiency. Women who have a high hemoglobin at term should be in better health and be better able to withstand hemorrhage and infection than those whose hemoglobin is low, and the administration of iron to pregnant women is therefore "a valuable and inexpensive preventative measure worthy of general application."—F. E. HYTTEN

The Anemias of Pregnancy in Dublin. P. B. B. Gatenby. *Proc. Brit. Nutrition Soc.* 15: 115, 1956.

Dublin, a city of over half a million, is served by three large maternity hospitals and over 80 per cent of the pregnancies in the city are cared for by these hospitals. These women usually return to the same hospital on each successive pregnancy, and each maternity center over a chosen number of years has its own group of patients which is fairly constant.

Inadequate diet is an important cause of iron-deficiency anemias in pregnancy in Dublin. Nevertheless,

iron therapy itself is effective in the individual case and there is some suggestion that iron therapy in one pregnancy will prevent or ameliorate iron deficiency in the subsequent pregnancy; presumably by replenishing depleted stores.

An inadequate diet is not likely to be the cause of megaloblastic anemia of pregnancy, at least in European climates. Temporary failure to utilize certain hematopoietic factors is a more probable explanation of this disease.—B. SURE

Nutritional and Intestinal Factors and Iron Losses in the Genesis of Tropical Anemias. H. Foy and Kondi. *Lancet* 1: 423, 1956.

Hypochromic microcytic iron-deficiency anemias are more common in the tropics and subtropics (particularly coastal and riverine areas of Africa and India) than the nutritional megaloblastic anemias.

Their etiology is briefly discussed. They often occur in areas where the diet contains adequate amounts of iron, and three possible factors are suggested. (1) There may be loss of blood from hookworm infestation; this is not considered an important cause. (2) In rice-eating areas the diet, which has a high phytic phosphorus content, may impair absorption and other unsuitable diet may upset the intestinal flora sufficiently to interfere with the absorption of essential nutrients. (3) Iron losses, particularly in sweat, have been calculated to greatly exceed the commonly accepted losses by this route.

These anemias usually respond well to oral iron but in some patients, often with abnormal serum protein levels, additional dietary protein may be required.—F. E. HYTTEN

Iron deficiency is frequently produced by a combination of excessive losses through occult bleeding with inadequate intake or malabsorption. Ferrous sulfate is still considered the treatment of choice and should be administered with about 100 mg of ascorbic acid. Parenteral iron therapy is effective, although toxicity must be avoided.

Oral Iron Compounds. A Therapeutic Comparison. D. J. O'Sullivan, P. G. Higgins, and J. F. Wilkinson. *Lancet* 2: 482, 1955.

Conflicting claims have been made for the efficacy of various forms of oral iron preparations in correcting iron-deficiency anemia, but many have been based on the treatment of the anemia of pregnancy, which often corrects itself post partum, and few studies have been adequately controlled.

The 80 subjects of this experiment had hypochromic, microcytic iron-deficiency anemia with a hemoglobin of less than 12.0 g per 100 ml mean corpuscular hemoglobin concentration (M.C.H.C.) of less than 30 per cent, and the hematogram and myelogram compatible with a diagnosis of iron deficiency. They were free from such complications as malignant disease, and the groups were comparable in terms of age, sex, and hemoglobin level. Anemia of pregnancy was excluded. The test continued for 6 weeks or until the hemoglobin had increased to 13.3 g per 100 ml.

Four compounds were compared: ferric hydroxide, ferrous sulfate, ferrous succinate, and ferrous gluconate, and they were administered in tablet form so that each patient received 70 mg of iron three times daily after meals.

All the ferrous compounds produced practically the same result—an increase in hemoglobin of about 1.2 per cent per day, but ferric hydroxide caused a hemoglobin increase of only 0.12 per cent daily. Figures shown for the increase in both M.C.H.C. and for serum iron give essentially the same result.

Intolerance, in the form of nausea and vomiting, to one or another compound (but never to all) was observed in five patients. Three of 23 subjects were intolerant to ferrous sulfate, but tolerated the gluconate, one out of 25 patients was intolerant of the gluconate but tolerated the succinate, and one out of 25 patients was intolerant of the succinate but tolerated the gluconate.

Out of an original 89 patients in the series, seven were completely refractory to oral iron; they responded well to parenteral iron.

Since ferrous sulfate in Britain is considerably cheaper than the organic iron compounds, it is considered that it should be used as the routine treatment of iron-deficiency anemia.—F. E. HYTTEN

Intramuscular Iron in Infancy. W. Gaisford, and R. F. Jennison. *Brit. M. J.* 2: 700, 1955.

This is a detailed report describing the use of "Imferon," an iron-dextran complex, in infants. In 21 infants, between 2 and 27 months of age, with "nutritional anemia," iron deficiency was confirmed by examining marrow from the iliac crest. Between 150 and 500 mg of iron were administered in doses of 50 mg (1 ml of "Imferon"). Fourteen babies with "anemia of prematurity" were similarly treated; in addition, 2 series of 10 prematures—one treated, the other observed as a control, were used to study the prophylactic value of the compound. A further 10 "surgical" cases are included.

The compound produced a rapid and sustained hematologic response; it is successful in correcting the "anemia of prematurity" and appears also to be a satisfactory prophylactic. It was given into the buttock and produced no ill effects.—F. E. HYTTEN

An Experimental Study of the Toxicity of Ferrous Gluconate. J. O. Hoppe, G. M. A. Marcelli, and M. L. Tainter. *Am. J. Med. Sc.* 230: 491, 1955.

The systemic and local toxicity of ferrous gluconate was determined in direct comparison with ferrous sulfate following intravenous and oral administration in experimental animals. In the acute intravenous study, there was no difference in toxicity in terms of iron content, although in terms of absolute weights of the salts

the toxicity of ferrous gluconate was about half that of ferrous sulfate. Delayed deaths of the animals were significantly greater with the latter salt. Following oral administration, delayed deaths were not of significance with either salt; ferrous gluconate was only one-third as toxic as ferrous sulfate in these experiments. Local gastric irritation and diarrhea occurred more promptly with ferrous sulfate. With intracutaneous injection, twice as much ferrous gluconate was tolerated before serious local tissue irritation occurred as could be tolerated with the sulfate salt. The magnitude of the acute oral toxicity values indicates a low order of absorption from the intestinal tract. Gastric lavage, along with supportive therapy for shock, is advised as an effective measure when spontaneous vomiting does not occur after toxic doses of the salts. These studies indicate that ferrous gluconate is less irritating and toxic than ferrous sulfate in terms of total weight of the drugs or in terms of their iron contents.—C. R. SHUMAN

Although the addition of cobalt to a parenterally administered iron compound raised the rate of hemoglobin formation, the toxicity and side-effects which may attend its use have limited its use clinically. An increase in iron absorption and utilization in infants induced by copper has been claimed; these results have not been confirmed.

Cobalt with Iron in the Treatment of Iron Deficiency Anemias. K. U. Jhatakia. *J. Indian M. A.* 26: 126, 1956.

Twenty-five cases of hypochromic anemia (17 microcytic, 4 macrocytic, and 4 normocytic) were treated with an intravenous preparation containing 100 mg saccharated iron oxide with 5 mg of cobalt in 5 ml. The dosage scheme varied from 9 to 28 days, and the total dose varied from 45 to 174 ml. The average daily rise in hemoglobin per 100 mg metallic iron with 5 mg cobalt was 2 per cent; when iron alone was used in a previous similar study the daily rise averaged 1.6 per cent.

The drug combination is said to be safe and free of untoward reactions. The author feels that iron plus cobalt intravenously produced somewhat better results than iron alone.

The variable degree of anemia, and the fact that some cases were ascribed to hookworm disease and hemorrhage and others to nutritional deficiency make it difficult to evaluate this report.—S. O. WAIFE

The Role of Trace Elements in Hemopoiesis and in the Therapy of Anemia. J. A. Bush. *Pediatrics* 17: 586, 1956.

Copper, cobalt, zinc, manganese, molybdenum, and possibly titanium and vanadium constitute trace elements which are present in the hemopoietic tissue. A deficiency of at least two of these elements—which is very difficult to produce in view of their small requirements—causes anemia in animals. The current status of knowledge of copper, cobalt, and molybdenum has been summarized by the author.

Copper deficiency in animals causes microcytosis and hypochromia with normoblastic hyperplasia of the bone marrow. In spite of iron administration (30 mg/kg), a decrease in iron concentration in the plasma occurs in copper deficiency and the copper content of plasma and erythrocytes is diminished.

Iron absorption is impaired in the presence of copper deficiency; however, parenteral iron administration does not alter the anemia or the changes in cell morphology; also, the erythrocyte survival time of copper-deficient erythrocytes is significantly decreased and is attributed to an intracorpuscular defect.

Surprisingly, hypercupremia was observed in 24 infants with iron-deficient anemia. Hypocupremia in association with iron deficiency occurs rarely if ever. Iron alone is required for the treatment of iron-deficient anemia.

In a study of a variety of clinical conditions, hypocupremia was observed in the newborn and in patients with hepatolenticular degeneration, nephrotic syndrome and severe hypoproteinemia. Normal plasma copper levels were observed in nutritional disorders including cirrhosis, scurvy, malnutrition, iron deficiency, and nutritional hypoalbuminemia.

The copper excretion in urine was increased in the nephrotic syndrome and correlated with the degree of proteinuria. The plasma and erythrocyte copper was decreased in a majority of cases and a significant anemia was present. No response followed copper therapy.

In three out of four cases with sprue, the copper concentration of the plasma was decreased and the value of copper as a therapeutic agent could not be assessed.

Cobalt is a part of the molecule of vitamin B_{12} and for this reason is essential for hemopoiesis. Ruminants synthesize vitamin B_{12} in the rumen and, therefore, parenteral cobalt is ineffective in correcting cobalt deficiency in such animals. Also polycythemia in many species is associated with excessive intakes of cobalt and has been attributed to an inhibition of a number of enzyme systems such as tyrosine iodinase, various oxidase and dehydrogenase systems, and catalase. The average diet contains more than the average requirements of cobalt (less than 5 μg); therefore, deficiencies are rare.

Cobalt in large doses, probably through its ability to produce polycythemia, has been used to treat anemia associated with chronic inflammation in humans such as chronic renal disease, malignancy, and infection. Certain side-reactions have been associated with its use, such as anorexia, nausea, vomiting, skin rashes, substernal pain, and even coronary occlusion. Cobalt-iron combinations have been claimed to be more effective than iron alone in the treatment of anemia of pregnancy, that of premature infants in the second and third month of life, and that of full-term infants. In sickle-cell anemia, a hemolytic anemia, cobalt has been efficacious; however, hypothyroidism with thyroid hyperplasia has been reported after the use of cobalt in

children with this disease and also in adults with chronic renal disease.

Because of the toxic effect of cobalt and the minor nature of many anemias which may not require treatment or may respond to safer agents such as iron, its use is not warranted. In chronic renal disease, malignancy, sickle-cell anemia, thalassemia, and aplastic anemia, further evaluation is in order.

Molybdenum deficiency has not been reported in man or animals and its role in hematopoiesis is not known. There is suggestive evidence that molybdenum is antagonistic to copper. There is no conclusive evidence that molybdenum possesses any advantage over iron in the treatment of iron-deficiency anemia or the anemia of prematurity.—J. N. ETTELDORF

RIBOFLAVIN

Unlike thiamine, the requirement for riboflavin does not seem to be related to caloric intake or muscular activity. However, there is a relationship between riboflavin metabolism and alterations in nitrogen balance. A reduction in urinary excretion of riboflavin accompanies nitrogen retention while more is excreted during periods of protein loss. For this reason it has been suggested that the daily riboflavin allowances be computed on the basis of the protein intake. Riboflavin deficiency may occur in the presence of a diet restricted in dairy foods or other meat products; or in excessive removal of the vitamin in cooking water, or upon exposure to light during cooking. Some of the clinical aspects of ariboflavinosis are discussed in the following report.

Observations and Research on Riboflavin Deficiency in Children. M. Gerbasi and G. R. Burgio. *Scientia Med. Italica* 4: 51, 1955.

The authors present their observations (including eight color plates) on ariboflavinosis in 39 children ranging from infancy to age 10 years. Both sexes were equally affected. The patients came from the lower economic levels and the incidence was found to be greatest in the fall, in conjunction with prolonged enteritis and diarrhea. Among the clinical findings are cheilosis, rhagades (angular fissures), scrotal patches of irregular pigmentation, magenta-red discoloration of the tongue and buccal mucosa, and hyporiboflavinuria.

Although these changes responded to riboflavin therapy, other signs required the addition of other members of the vitamin B complex and are presumably produced by other deficiencies. These include large deep fissures in various flexural parts (axilla, elbow, groin) with a surrounding dry brown skin; palpebral erythema and a pellagra-like erythema on the back of the elbow and knee, and buttocks. Anemia, which was present in 23 subjects, was hyperchromic in twelve, normochromic in nine, and hypochromic in two. Bone marrow examination showed an increase in the diameter of cells and nuclei in the granulocytic cells as compared to normals of the same age. There was an increase in immature forms of the granulocytic series, and a variable number of megaloblastic cells whose morphology was intermediate between normo- and megaloblasts.

There were electrocardiographic suggestions of myocarditis, as well as laboratory and histologic evidences of hepatic involvement, especially steatosis, in the more severe cases. Hypoproteinemia was seen with an increase in gamma-globulin but a normal or reduced beta-globulin. Ketonemia and reduced peripheral utilization of glucose were also found.

Aureomycin, in addition to vitamin and dietary supplementation, appeared to produce best results. The original paper gives some details on therapy. The authors conclude that the clinical picture may be analogous to kwashiorkor in tropical areas. (As noted by the authors, however, the concomitant presence of severe prolonged diarrhea complicates this picture of "pure" riboflavin deficiency).—S. O. WAIFE

The best sources of riboflavin are dairy products; a mixed diet containing a pint of milk is likely to provide an adequate intake of the factor.

Riboflavin in Milk. V. V. Modi and E. C. Owen. *Nature* 178: 1120, 1956.

The partition of riboflavin between free riboflavin, flavin mononucleotide and flavin adenine dinucleotide was studied in the milk of seven species. Chemical methods are briefly described.

In the milk of cows, goats, ewes and rabbits riboflavin was found both free and as the flavin adenine dinucleotide. In human, mare and sow milk only flavin adenine dinucleotide was found sometimes with traces of free riboflavin and flavin mononucleotide which may have been formed by hydrolysis from the flavin adenine dinucleotide.

Ultrafiltrates of the milk did not contain flavin adenine dinucleotide suggesting that either the molecule was too large to pass the membrane or that it is in a bound form.—F. E. HYTTEN

The current methods for assaying riboflavin are the microbiologic technic of Snell and the chemical assay which depends upon fluorescence of the vitamin under carefully controlled conditions. A number of flavoprotein enzymes systems are under investigation, each containing a specific protein carrier and a riboflavin prosthetic group. These are essential components of the oxidative systems within living cells.

Dietary Deprivation of Riboflavin and Blood Riboflavin Levels in Man. O. A. Bessey, M. K. Horwitt, and R. H. Love. *J. Nutrition* 58: 367, 1956.

The development of practical microchemical analytical methods for riboflavin, flavin mononucleotide (FMN), and flavin adenine dinucleotide (FAD), and the observation that the concentrations of some of these substances in the red blood cells, white blood cells and plasma of experimental animals vary with the dietary

intake of riboflavin, made it feasible to consider further the use of blood analytical methods for the evaluation of nutritive status in man, with respect to this dietary essential.

The total riboflavin in red blood cells, white blood cells and plasma, and the free plus FMN riboflavin and FAD riboflavin in plasma were determined on one group of 10 men who had been maintained for 16 months on a well-controlled dietary intake of 0.55 mg of riboflavin/day. Similar measurements were made on a control group of 6 men who had received 2.55 to 3.55 mg of riboflavin/day. The riboflavin content of the red blood cells was 10.0 to 13.1 μg/100 ml in the restricted group and 20.2 to 27.6 in the control group. Although the free and FMN riboflavin of plasma was in general decreased in the restricted group, there were some striking exceptions. The plasma FAD riboflavin and the total white blood cell riboflavin were not significantly changed.

Analyses of riboflavin in red blood cells were done on a group of 8 men before and periodically during a nine-month maintenance on a riboflavin intake of 0.5 mg/day. Similar analyses were done on four control groups receiving 1.6 to 2.4 mg of riboflavin daily. The riboflavin content of the red blood cells became significantly lower in the restricted group within 45 days of the restriction and slowly decreased further during the ensuing months. It is concluded that the red blood cell content of riboflavin is a reasonably sensitive and practical index for evaluating nutritive status with respect to this dietary essential and that available microchemical methods are well adapted for this measurement.—B. SURE

Riboflavin Level of the Blood of Normal Indian Male Adults and the Effect of Administration of Large Doses of This Vitamin on It. H. N. De, P. Datta and P. N. Mankad. *Ann. Biochem. & Exper. Med.* 15: 137, 1955.

Using microbiologic assay methods, the riboflavin content of the blood of 20 normal males from India was found to vary from 48 to 62 mcg (average 53 mcg) per 100 ml whole blood. Using urinary excretion to indicate saturation of the tissues with the vitamin, administration of 10-mg daily doses of riboflavin for a continued period of a week led to tissue saturation but did not affect the blood riboflavin level. The authors suggest that the constancy in the blood riboflavin level in this study is maintained at the expense of stored riboflavin in the liver and other storage tissues.—S. O. WAIFE

EFFECTS OF RADIATION UPON FOODS

Studies upon the use of irradiation of foods for their preservation and sterilization are of the greatest importance. The successful processing of foods such as meat, milk and vegetables by this method may facilitate storage and shipping problems in food technology. Many fundamental questions concerning the effect of irradiation upon the nutritive value of foods compared to that of refrigeration will have to be answered. At present, there are difficulties with odors, flavors and abnormal textures of foods sterilized by radiation. Before they can be safely consumed it must be determined that this type of processing of the foods exerts no deleterious effect upon the organism and that the wholesomeness of foods is unaltered.

Effect of Irradiation Sterilization on Nutritive Value of Protein and Energy of Food. B. C. Johnson and V. C. Metta. *Fed. Proc.* 15: 907, 1956.

The irradiation sterilization of various foods (beef, beans, peas and milk) did not produce a greater loss in the nutritive value of the protein content of these foods than occurs by other food-processing methods. Milk was found to be sensitive to irradiation, and the loss in protein value has been shown to be due to a loss in cystine, either by destruction or binding. There is evidence that although there must be some irradiation level at which the energy value of a food could be depressed, this level must be well above that required for sterilization.—S. O. WAIFE

Exposure to irradiation has significant effects upon gastrointestinal physiology. Such effects may occasionally be observed in patients receiving radio-therapeusis in the treatment of malignancy.

Effect of Total Body Irradiation on Absorption of Sugars From the Small Intestine. J. T. Farrar, M. D. Small, D. Bullard and F. J. Ingelfinger. *Am. J. Physiol.* 186: 549, 1956.

A study was made in rats on the effect of large doses of total body x-irradiation on the intestinal absorption of glucose, fructose and xylose administered intraduodenally. Irradiation caused a slight but highly significant decrease in absorption of all three sugars when given singly. These studies do not indicate selective inhibition of any specific mechanism involved in the absorption of these three sugars. No difference attributable to sex exists between the postirradiation absorption rates. When mixtures of the three sugars were given, a questionably significant decrease was noted in all absorption rates, with the exception of xylose in the female rats. In this group absorption of xylose was unaffected by irradiation. In rats not exposed to irradiation, the relative absorption rates of the three sugars are markedly different when given singly and when given in a mixture.—AUTHORS

Effect of Gamma Radiation on Gastric Emptying Time in the Dog. R. A. Conrad. *J. Appl. Physiol.* 9: 234, 1956.

The emptying time of the stomach was observed by using x-ray visualization of a barium meal. When dogs were exposed to 300–600 r the emptying time, was unchanged two to three days later. Control values were also observed to be unchanged seven to eight days after 300 r. However, when the exposure was increased

to 1300 r there was a marked delay in gastric emptying three days later. These same animals exhibited anorexia, retching, vomiting and diarrhea with apathy and dehydration. It should be pointed out that on the second day post irradiation the emptying time was normal and symptoms much less marked. The rat is different in that sublethal irradiation produces significant delay in sublethal ranges.—M. J. OPPENHEIMER

Effects of Irradiation on Wholesomeness of Mixed Organ Meats in Diet of the Rat. E. C. Bubl and J. S. Butts. *Fed. Proc.* 15: 930, 1956.

A study on rat longevity lasting for two years and four generations is reported. These animals were fed irradiated or non-irradiated organ meats. There were no adverse effects on growth reproduction.—S. O. WAIFE

Radiation Effects on Water Soluble Vitamins in Raw Beef. H. D. Alexander, E. J. Day, H. E. Sauberlich and W. D. Salmon. *Fed. Proc.* 15: 921, 1956.

The effect of gamma radiation on water-soluble vitamins of raw ground beef (frozen in cans) was evaluated. Values obtained by microbiologic or chemical methods compare favorably with each other. It was found that thiamine was significantly decreased (as much as two-thirds) by various methods. From 8 to 10 per cent of riboflavin and about 24 per cent of pyridoxine was destroyed by radiation. There was no detectable decrease in the content of niacin, choline and folacin.—S. O. WAIFE

Effect of Ionizing Radiations on Vitamin K. L. R. Richardson, P. Woodworth, and S. Coleman. *Fed. Proc.* 15: 924, 1956.

Menadione was more readily destroyed by ionizing radiations than either vitamin K_1 or K_3. When relatively large amounts of the three compounds were added to a diet, sufficient vitamin-K activity remained after irradiation to prevent the development of hemorrhage. The loss of vitamin-K activity was comparatively small when a diet containing a natural source was irradiated or when natural food was irradiated. Therefore, the authors conclude that no animal or man receiving irradiated diets composed of natural foodstuffs is likely to develop a hemorrhagic condition because of vitamin-K deficiency.—S. O. WAIFE

INSULIN

Among the most thoroughly studied agents in medicine is insulin whose complex protein structure has been completely dissected by the biochemists and whose metabolic effects have been exhaustively traced by physiologists. By promoting a single step in the initial phase of glucose metabolism, the transfer of glucose into the cell to form glucose-6-phosphate, a great array of transformations involving every phase of cellular activity are made possible. One of the important consequences of insulin action is the promotion of protein biosynthesis. Through the provision of energy supplied by glycolysis and the availability of hydrogen ions liberated in this same process, the formation of peptides and proteins by the cells is made possible. The protein anabolic effect of insulin is capable of supporting growth in certain hypopituitary subjects.

Insulin and Growth. D. Hubble. *A.M.A. Am. J. Dis. Child.* 90: 600, 1955. (Soc. Trans.)

Best and his co-workers have shown that a slow-acting insulin will maintain growth in hypophysectomized rats. All of the features of the Mauriac syndrome in diabetic children (five patients)—dwarfism, florid facies, hepatomegaly, obesity, hypercholesterolemia, and sexual infantilism—can be explained by the known effects of the corticosteroids. The pathogenesis of the syndrome depends on a deficiency of insulin, particularly during the night, which allows an enhanced activity of the corticosteroids. In one patient who died the large liver was filled with glycogen; in two patients treatment by long-acting insulin was shown by nitrogen balances to increase the retention of nitrogen, and this experimental observation has been confirmed by better-than-average growth in the succeeding two years. The regression of other features, such as hepatomegaly, can be explained by the recession of adrenocortical activity.

Hypopituitarism occurring in diabetic adolescents (two patients) is characterized by dwarfism and sexual infantilism and can be explained by defective anabolism of protein (insufficient insulin) or by increased breakdown of protein (gluconeogenesis by corticosteroid action). Hypopituitarism was overcome in both patients by the use of long-acting insulin with adequate control of the diabetes through the 24 hours.

In three dwarfs, two with presumed hypopituitarism and one of the Lorain type, no increased growth could be demonstrated by prolonged insulin therapy, although increased nitrogen retention had been demonstrated in nitrogen balances. In the two hypopituitary dwarfs, who had normal adrenocortical function, there was weight gain with increased fat deposition. This is presumably the difference between these patients and Best's hypophysectomized rats. Insulin does not fully overcome the protein-catalytic action of the corticosteroids.

It is concluded that insulin will promote growth in diabetic children with the Mauriac syndrome and in uncontrolled diabetic adolescents with hypopituitarism. In these latter patients the improved growth and developing sexual function may depend on improved protein anabolism associated with adequate insulin therapy; in the former group, growth depends on the depression of excessive adrenocortical activity. In dwarfs with normal adrenocortical activity insulin therapy does not promote growth.—J. N. ETTELDORF

The presence of glucose in the interstitial fluids of various tissues in high concentrations during hyperglycemic periods may account for the subsequent rise in

venous blood glucose levels. The negative A/V glucose difference has always been puzzling and can best be explained on this basis which should be readily susceptible to investigation.

The Effect of Insulin Administration on Arteriovenous Glucose Differences in the Alloxan-Diabetic Dog. D. E. Gray and H. A. DeLuca. *Canad. J. Biochem. & Physiol.* 34: 763, 1956.

It has been shown both in man and animals that, after the intravenous administration of insulin, the glucose concentration in the venous blood may exceed that in the arteries, giving a negative anteriovenous difference.

In the present experiments alloxan-diabetic dogs were given intravenous glucose (1 g/kg body weight), insulin (0.5 unit/kg) and both glucose and insulin together. A negative anteriovenous difference occurred in five of six animals after insulin (most marked after two hours) but the difference was much greater, and occurred in all six animals, after both insulin and glucose.

It is suggested that the mechanism may be that glucose goes into the interstitial fluids and when the blood glucose is lowered by insulin it returns to the blood stream, thereby raising the venous glucose level.—F. E. HYTTEN

The delayed disappearance of insulin from the serum of diabetic patients has very important connotations. This phenomenon can now be explained on the basis of the presence of a gamma globulin demonstrated by Berson et al. (J. Clin. Investigation Feb. 1956) to develop as an antibody which binds insulin and delays its reaching the cellular level. The insulin-binding globulin is formed in all subjects receiving insulin over several months of time. It is probable that this globulin developing in increasing concentrations may account for the elevated insulin requirements observed in certain patients.

The Distribution and Metabolism of Insulin Labeled with Radioactive Iodine (I^{131}) in Normal and Diabetic Subjects. G. W. Welsh, III, E. D. Henley, R. H. Williams, and N. J. Elgee. *Diabetes* 5: 15, 1956.

The authors report on the distribution and metabolism of insulin labeled with radioactive iodine (I^{131}) in 40 diabetics of varying type and severity, 15 healthy controls, and 11 other nondiabetics with various illnesses. The labeled insulin disappears less rapidly from the plasma of many diabetics as compared with normal controls and other nondiabetics. There is also less rapid degradation of labeled insulin by these diabetics as compared with controls. Finally, there is no apparent correlation between these observations and the clinical characteristics of the diabetics.

This is a very interesting study and brings up more problems to be answered. Preliminary *in vitro* studies reported by the authors suggest that in diabetics the "unsaturation" of plasma components with insulin may be responsible in part for the apparent retention of the labeled insulin. This will be an excellent technic to combine with insulin assay when the latter technic is available.—K. R. CRISPELL

Inhibition of Insulin Action by Serum Gamma Globulin. A. R. Colwell and R. W. Weiger. *J. Lab. & Clin. Med.* 47: 844, 1956.

The authors present a very interesting study on a patient with hemochromatosis and resistant diabetes followed over a seven-month period. There was extreme resistance to insulin with the requirement increasing progressively to 11,400 units daily. This was associated with hypergammaglobulinemia. Both phenomena were reduced almost to normal by the administration of corticotropin.

The gamma globulin fraction of the serum showed insulin-inhibiting titers comparable to those of the sera from which they were prepared. They conclude that the serum gamma globulin of the patient contained an unknown substance which inhibited the insulin effect up to the point of excessive dosage. They offer several theoretic possibilities for the presence of the hypergammaglobulinemia and the substance causing insulin resistance. This is a carefully planned piece of work and should create further interest to unravel the problem of insulin resistance.—K. R. CRISPELL

An Investigation of Prolonged Insulin Resistance in a Case of Diabetes Mellitus. J. R. Presland and C. M. Todd. *Quart. J. Med.* 25: 275, 1956.

An obese 57-year-old diabetic woman is described who had controlled her diabetes for 12 years with 40 units of insulin daily. A month following treatment for a furuncle on the hand she developed an increasing insulin resistance and was admitted to hospital in diabetic coma. Insulin requirements increased after recovering from coma to as much as 5,000 units daily during the fourth week in hospital, after which they declined and she left hospital after 19 weeks on 600 units. She died nine months later of coronary thrombosis.

The remarkable feature of the case was the presence of a large amount of insulin associated with the β-lipoprotein of the blood plasma. The woman's serum induced hypoglycemia in the rat and stimulated glycogen formation in isolated rat muscle. The evidence suggests that the resistance to insulin was due to a defective response in the tissues.

Changes in the plasma protein spectrum ran parallel with the declining phase of insulin requirement, but there is no evidence that the two events were related.—F. E. HYTTEN

Additional observations are accumulating to support the concept of action of insulin proposed by Levine. It appears that the primary effect is that of promoting the transfer of glucose across the cellular membranes.

The Action of Insulin on the Penetration of Sugars into the Perfused Heart. R. B. Fisher and D. B. Lindsay. *J. Physiol.* 131: 526, 1956.

The isolated heart of the rat was used in these studies. It has been demonstrated that a major action of insulin, in heart muscle at least, is to facilitate the entry of glucose into muscle cells. These studies show that galactose penetrates into intracellular water. However, the perfused rat heart does not use this sugar. The rate of penetration of galactose is not a linear function of its external concentration. Entrance of galactose into cells is increased by insulin in ranges of 0.2–2.0 mU per ml. Glucose decreases the rate of penetration. On the other hand, galactose decreases the rate of glucose utilization. Insulin and sorbitol remain extracellular in heart water. When glucose and sorbitol spaces are compared, it is observed that insulin causes an increase of intracellular glucose.—M. J. OPPENHEIMER

One of the most significant advances in diabetic therapy in recent years has been the development of the intermediately acting insulins, NPH and Lente. The following reports on the Lente preparations attest to its clinical usefulness. Over 80 per cent of diabetic patients are satisfactorily controlled by a single dose. The remainder can usually be stabilized either on a split dose or on the intermediate insulin with unmodified insulin added to it.

Insulin Zinc Suspension. Four Years' Experience. M. Jersild. *Lancet* 2: 1009, 1956.

Experience with insulin zinc suspensions ("Lente" insulins) (I.Z.S.) is reported for 1,000 diabetic patients comprised of, 512 males and 488 females of all ages. Ninety per cent of them were admitted to the hospital for initial adjustment to the new insulin and about 96 per cent were followed up for an average of 18 months.

The results are presented and discussed in detail. Ninety-six per cent of the patients were controlled on one daily injection of the I.Z.S. suspensions with an average dose of 40 units; 12 per cent had added amorphous I.Z.S. (the quick-acting "Semi-lente") and 8 per cent had added crystalline I.Z.S. (the long acting "Ultralente") in the single injection. The amorphous or crystalline suspensions were used alone only in exceptional cases. The remaining 4 per cent required two daily injections.

After 18 months 82 per cent of the single injection patients were still maintained on this regime and 19 per cent of the group which originally required two injections had later been transferred to a single daily injection. "With preparations of I.Z.S. the results were satisfactory, even in most cases, where control had previously been difficult."—F. E. HYTTEN

Lente Insulin. Four Years' Experience. A. G. Spencer and M. E. Morgans. *Lancet* 2: 1013, 1956.

The addition of small amounts of zinc to insulin in an acetate buffer depresses the solubility of the insulin and prolongs its absorption from the site of injection. By adjustment of the pH a quick-acting amorphous insulin ("semilente") and a long-acting crystalline preparation can be made ("ultralente"). These suspensions can be mixed. In the proportion of 30 per cent amorphous to 70 per cent crystalline, they form the preparation "Lente" insulin (I.Z.S.).

Experience with use of I.Z.S. for at least six months in 200 patients is reported in detail. Eighty-three per cent of the patients were controlled satisfactorily by I.Z.S. and in 36 per cent the control was improved. Treatment was abandoned in nine patients: four felt better on their previous treatment; they did variable daily work and were better controlled by two injections of P.Z.I. and S.I.; three patients had recurring hypoglycemia on I.Z.S. and two patients, one who developed tuberculosis and another who always became unbalanced with minor injections, were better controlled by a two-injection regime.

Seven patients who had had local reactions to the injection of P.Z.I. or globin insulin had no reaction to I.Z.S., but one patient developed a well-marked fat-atrophy at the site of injection. There were only 11 children and adolescents and two pregnant diabetics in the series. Treatment with lente insulin was very satisfactory in all of them.—F. E. HYTTEN

HEPATIC DISEASE: NUTRITIONAL ASPECTS

In the treatment of patients with liver disease emphasis has been given to the feeding of diets rich in protein sources, with vitamin supplements. Other dietary modifications such as fat restriction have gradually been abandoned for a more normal distribution. It is likely that the advocacy of a high-protein diet must also undergo modification, particularly for those patients with chronic liver disorders. During recent years such diets have been found to be associated with an elevation of plasma ammonia levels and occasionally with mental symptoms.

Observations on the Source of Elevated Plasma Ammonia Levels in Hepatic Insufficiency. H. L. Zimmerman, R. J. Korn, and H. G. Weinstein. *Am. J. Med. Sc.* 231: 177, 1956.

Plasma ammonia levels were determined in 66 patients with cirrhosis, 40 patients with hepatitis, 16 with hepatic coma, and in 60 patients without evidence of liver disease. Additional procedures employed in this study included observations on the effect of ammonium chloride on blood ammonia levels, variation of protein intake in a patient with porto-caval shunt, and the effect of chlorotetracycline upon blood ammonia levels following glycine or gelatin feeding. The plasma ammonia levels were elevated in the hepatic coma cases as well as in certain of the non-comatose patients with cirrhosis or hepatitis. There were many non-comatose patients with higher ammonia levels than in some of those who were comatose. Apparently

elevated plasma ammonia is the most consistent biochemical abnormality observed in hepatic coma; however, a pathogenetic relationship of this disturbance to coma remains to be proved. Impaired tolerance to ammonium chloride was demonstrated in patients with cirrhosis. A high-protein intake was consistently associated with a mounting ammonia level and usually with mental symptoms. A consistent suppressive effect of tetracycline on plasma ammonia could not be demonstrated.—C. R. SHUMAN

The present evidence suggests that ammonia is derived from dietary or gastrointestinal sources and that the normal liver removes this compound from the portal blood. Lipotropic compounds such as methionine may represent an additional source of ammonia. In the following, a test for ammonia tolerance using ammonium chloride has been introduced.

Critical Study of Blood Ammonia Level in the Course of Hepatic Disease. A. Varay and M. Masson. *Arch. d. Mal. de l'app. Digestif* 45: 5, 1956.

After evaluating available methods of measuring blood ammonia, and confirming the value of Conway's technic, the authors discuss the significance of blood ammonia levels in hepatic disease.

Blood ammonia levels below 0.50 per cu mm were found in all normal subjects studied. In cirrhosis with ascites, levels were above normal in 16 out of 17 cases. The extent of the rise did not correspond with the degree of development of the cirrhotic process, nor with the presence of neurologic signs. It did, however, appear to be associated with the amount of collateral circulation or signs of portal hypertension. In grave hepatic insufficiency with coma, blood ammonia levels were considerably higher than normal in all six of the authors' cases (lowest 0.86, highest 1.86 per cu mm), but there was no relationship between depth of the coma and extent of the rise in blood ammonia. The authors have noted levels almost equally high in cirrhosis without coma, and they therefore feel that the prognostic value of a high level is not absolute. In two patients with jaundice due to hepatitis, levels were within normal limits; they were normal, too, in two cases of obstructive jaundice in one of "cardiac" cirrhosis, and in two of liver sclerosis without ascites.

The intravenous administration of calcium glutamate in two cases, considerably lowered the high ammonia levels but did not produce lasting clinical benefit.

The effect of loading doses of ammonium salts was also investigated. After ammonium chloride administration, blood ammonia levels remained within or only slightly above normal limits in all of the normal subjects tested, with the exception of one subject who had had hepatitis six months earlier. In all eight of the cirrhotic subjects tested (all with ascites), blood levels of ammonia, abnormally high before the loading dose, showed a considerable further rise, usually at the end of 60 or 90 min. Even at 180 min, values were almost always higher than the pretest levels. In two cases of obstructive jaundice, ammonia levels remained normal, but in two cases of jaundice due to hepatitis, a slight elevation was produced by the loading test. The authors conclude that the loading test offers a valuable means of demonstrating the presence of a disturbed portal circulation and in differentiating between obstructive and nonobstructive jaundice.

Walshe's theory is that a deficient hepatic mechanism is responsible for the hyperammonemia of hepatic coma. These authors, however, feel that available experimental evidence, such as the occurrence of "meat intoxication" in animals with Eck fistulae, lends stronger support to the hypothesis of a vascular derivation of the excessive blood ammonia, chiefly via the portal vein and the rich collateral portal circulation which develops in cirrhotic subjects. The fact that blood ammonia is not elevated in experimental liver intoxications (with carbon tetrachloride, chloroform, etc.) is also suggestive.

Clinical implications of these studies are that high protein regimens, rich in meat, should be used with extreme caution in hepatitis and cirrhosis; perhaps it would be wise, too, to restrict lipotropic amino acids like methionine. The results of the loading test, as described here, can be useful in guiding the clinician to the proper dietary decisions. Obviously, in the light of these findings, the use of ammonium chloride as a preliminary to the administration of diuretics to cirrhotic patients should be avoided.—C. J. HOWELL

In the preceding and following, the use of glutamine in treatment of hepatic coma has not been successful. Some of the reasons for the failure of this therapy are discussed.

Glutamine and Ammonia During Hepatic Coma. M. V. Schwarzmann. *Arch. d. Mal. de l'appl. Digestif* 45: 32, 1956.

Recent efforts to implicate a failure of the liver in the increased blood ammonia level and the neurologic disturbances observed in hepatic diseases have made the assessment of ammonia metabolism an object of considerable clinical interest. The difficulties inherent in the measurement of ammonia levels in the blood make even the preferred method (Conway's microdiffusion technic) hard to carry out in ordinary clinical practice. The various technical problems connected with Conway's technic and its modifications are analyzed in this helpful paper. Like others, this author has found no strict parallelism between severity of clinical signs and blood ammonia values; some comatose cirrhotics have normal values, while high levels are sometimes found in noncomatose cirrhotics. For the various theoretic and practical reasons outlined, Schwarzmann decided to approach the metabolic problem of hepatic coma by way of glutamine. Glutamine represents 20 to 40 per cent of the total protein nitrogen in the blood; it is easily deaminated; its role in the transport of ammonia ions is well established; after the kidney, the

liver and brain are the organs richest in glutaminase, although the exact role of hepatic and cerebral glutaminase has not been elucidated; finally, liver cells are extremely permeable to glutamine, suggesting that the liver is an important locus of its metabolism.

Normal glutamine values were found in all patients studied, including all cases of cirrhosis uncomplicated by coma. In contrast, quite striking elevations were found in all but 3 of 12 cases with hepatic coma. ("Hepatic coma" is here strictly defined so as to exclude all cases explicable in terms of electrolyte imbalance, neurologic manifestations of alcoholism, etc.; it is applied only to the clinical picture of severe, progressive, fatal hepatic insufficiency.) In the three comatose patients on whom blood ammonia determinations were also done, an elevated ammonia level accompanied the rise in plasma glutamine. Unfortunately, it was not possible to determine blood NH_3 in the three patients in whom, despite coma, the glutamine level was normal; however, whenever both determinations were carried out, a striking parallelism was observed.

Attempts to treat hepatic coma by glutamine administration have failed. This might be expected from the fact that the plasma glutamine level is already high, although the accumulation of a substance in the blood does not necessarily prove that it is present in excess in the body, since it may equally well reflect non-utilization. The reason for the increase in plasma glutamine remains to be explained.

Schwarzmann concludes that no hypothesis so far advanced—including the claim that coma is the result of excess ammonia accumulation—is susceptible of clinical verification. It is the author's view that the biochemical and enzymatic disturbances responsible for the onset of hepatic coma are exceedingly complex, and that the observed increases of ammonia and glutamine are only "fragmentary and often deceptive reflections" of a process not yet understood.—C.-J. HOWELL

The Treatment and Prognosis of Hepatic Coma. S. Sherlock, W. H. J. Summerskill, and A. M. Dawson. *Lancet* 2: 689, 1956.

Coma has been regarded as a very serious and usually terminal complication of liver disease. Recently it has been shown that the reduction of dietary nitrogen and treatment with antibiotics are beneficial. This paper reports 66 cases of liver disease with coma treated along these lines. The intestines were emptied and kept free of all nitrogen-containing material; chlortetracyline was given and "any precipitating factor was energetically treated."

Thirty-nine of the subjects, 12 of whom had been in acute deep coma, recovered. Thirteen patients with chronic neuropsychiatric changes were maintained on low-protein diets for up to two years without obvious protein malnutrition. Intravenous sodium glutamate was given to 12 patients without clinical improvement.

The prognosis was better in cirrhosis than in acute virus hepatitis and there is an advantage in beginning treatment in the pre-comatose stage. Outlook was improved when some clear precipitating factor such as gastro-intestinal hemorrhage could be treated. Seven of eight patients with cirrhosis who recovered from deep coma were alive a year later.—F. E. HYTTEN

In experimental hepatic fibrosis and in nutritional cirrhosis described from various areas an important conditioning factor in pathogenesis is the presence of concomitant infection or parasitic infestation associated with dietary inadequacy. Some experimental observations are recorded.

Studies on the Genesis of Experimental Diffuse Hepatic Fibrosis. I. MacDonald, and G. A. Thomas. *Clin. Sc.* 15: 373, 1956.

Two groups, each composed of three male and three female adult rabbits were maintained on two diets. One consisted of 13.6 per cent casein hydrolysate, 81.4 per cent sucrose and 5 per cent of a salt mixture with added yeast and a concentrate of vitamins A and D: the other contained 31.7 per cent casein at the expense of sucrose. The diets caused a progressive loss of weight. The rabbits were killed at intervals of about two weeks. The livers were examined and are described in detail.

Fatty infiltration of the parenchymal cells first around the central vein and then spreading peripherally was obvious at 15 days on the first diet and became progressively worse with time. This was also obvious on and after 29 days on the second diet. Fibrosis, both peri-portal and to a lesser extent centri-lobular, and proliferation of bile duct epithelium occurred in both diets, and increased with time.

Total lipid in the dry liver reached 30 per cent in one animal but was generally below 20 per cent; the iodine number was variable and suggested that the liver lipid was not merely transferred depot fat. The genesis of the hepatic lesions is discussed and it is suggested that they may be the reaction to both dietary inadequacy and infection with the parasite *Eimeria stiedae*.—F. E. HYTTEN

Investigations into the Aetiology of an Experimental Nutritional Hepatic Fibrosis. I. MacDonald, and G. A. Thomas. *Clin. Sc.* 15: 389, 1956.

The effect of adding separately a variety of nutrients to the two diets described above was studied in an attempt to discover the specific inadequacy causing the liver lesions. The additions were yeast, choline, vitamin B_{12}, dried hog's stomach, tocopherol, cellulose, linoleic acid, barley shoots, and parenteral protein. Coprophagia was permitted in another experiment. Hepatic changes were not histologically different from those previously described. The extent of the liver damage appeared to be related to the degree of coccidial infection. It was not possible to reproduce these liver lesions in five rats fed the two basic diets for 490 days.—F. E. HYTTEN

Hepatic Fibrosis Produced with a Fat Free Diet. I. MacDonald, and G. A. Thomas. *J. Physiol.* 131: 25P, 1956.

Diffuse hepatic fibrosis was produced in the rabbit by a diet of 31.7 per cent casein hydrolysate, 63.3 per cent sucrose, 5 per cent salts mixture, dried yeast, vitamin A, and vitamin D. In rats on the same diet liver lipids increased slightly but there was no fibrosis. Coccidial infection plays a role since lightly infested rabbits show only a slight change in liver on the same diet. Histologic changes in the rabbits are similar to those in west African children with chronic malaria. Combined infestation and inadequate diet cause fibrosis, but either alone does not. There is a close relation between plasmodium and the parasite *Eimeria stieda* which infests rabbits.—M. J. OPPENHEIMER

Jaundice associated with liver or biliary tract disease may interfere with fat absorption leading to steatorrhea and impaired calcium absorption. These abnormalities may lead to bone disease the incidence of which has not been generally appreciated.

Malabsorption and Bone Disease in Prolonged Obstructive Jaundice. M. Atkinson, B. E. C. Nordin, and S. Sherlock. *Quart. J. Med.* 25: 299, 1956.

A study was made of 25 patients who had suffered from obstructive jaundice for three months to seven years. Three were suffering from hepatocellular jaundice, the other 22 from bilary obstruction.

Fat balances were estimated in 18 patients; all had demonstrable steatorrhea. There was an inverse relationship between fat-absorption and fecal stercobilinogen and between the latter and serum bilirubin.

Nitrogen output was normal in the 15 patients investigated. The skeletal status was studied in 24 of the 25 subjects. In eight the skeleton appeared to be normal and four were suffering from possible early osteomalacia. Seven subjects were suffering from established osteomalacia confirmed by both biochemical and histologic investigation and there was possibly some osteoporosis as well. Three patients were considered to be suffering from osteoporosis only and the remaining two from both osteomalacia and osteoporosis.

Treatment with intramuscular vitamin D (300,000 units in four weeks) appeared to cure one case of osteomalacia and relieved bone pains in another. In one other patient the osteomalacia was halted and in two others it deteriorated.—F. E. HYTTEN

The influence of x-irradiation upon certain aspects of liver function leading to elevated aminoacidemia may be involved in such side-effects as nausea, anorexia, and malaise experienced by occasional patients.

Liver Function in the Chick Following X-Irradiation Plasma Amino Acids and Plasma Glucose. E. K. Bernstein, S. P. Stearner and A. M. Brues. *Am. J. Physiol.* 183: 543, 1956.

Abnormal levels of some plasma constituents influenced by the activity of the liver were studied in 3-day chicks after single dose x-irradiation of 1000 r, given at 43 r/min. An approximately two-fold increase in total plasma amino acid concentration was observed at one hour following x-irradiation and an approximately three-fold increase at three hours following x-irradiation. Although the average increase over control values at five hours was the same as at three hours, some individual values increased to about four times the control level. Concurrently, total plasma protein decreased. There is a lack of correlation between the condition of the irradiated animal and the amino acid level or number of amino acids; increased levels occurred at one hour following x-irradiation in animals which appeared normal at autopsy.

A similar alteration in amino acid levels has been reported in man immediately following x-irradiation; this seems to be an extremely sensitive radiation response. Mean plasma glucose levels determined in newly hatched chicks at one, three, and five hours after x-irradiation showed no significant changes from control levels. Individual animals, however, showed a hyperglycemia of 50–100 mg/per 100 ml over control values at three and five hours following x-irradiation. Such hyperglycemia was usually found in sick birds and was commonly associated with liver hemorrhages.—AUTHORS

DIET AND DIABETES

In diabetes, the rate of lipogenesis may be decreased and the oxidation of glucose to carbon dioxide diminished. Without these two important pathways of disposal of acetyl groups available, the formation of cholesterol is markedly enhanced as the levels of acetoacetate increases. This derangement can be improved by administration of insulin and by reduction of fat intake.

Serum Lipids in Diabetic and Non-Diabetic Rats, Effect of Varying Lipid Diets. R. N. Cagan, R. Nichols. and L. Loewe, *Diabetes* 5: 112, 1956.

The authors have investigated the effect of varying lipid diets on the serum lipids in diabetic (alloxanized) and non-diabetic rats.

Both the normal and the diabetic rats had a marked elevation of their serum lipids while on a high-fat diet. Diabetic animals on a control diet have an elevation of total fatty acids. The significant finding was that diabetic animals on a high-fat diet had a significant elevation of total cholesterol and lipid phosphorus above the control rats on the same high-fat diet. The increase in fatty acids was about the same.

The authors offer the interpretation that the surplus exogenous fat in the form of fatty acids fed to these animals is broken down and resynthesized to cholesterol. This is based on the experimental evidence that in the diabetic animal fatty acid synthesis but not cholesterol synthesis is impaired.

This is an interesting experiment and an important observation that suggests that the high-fat diet in the management of diabetes needs re-evaluation.—K. R. CRISPELL

The remarkable results reported below with a low-fat dietary program in diabetes mellitus require confirmation. I have prescribed similar diets in a group of unstable diabetics with hypercholesterolemia without observing a pronounced change in the insulin requirements.

Low-fat Diet and Therapeutic Doses of Insulin in Diabetes Mellitus. L. Singh. *Lancet* 1: 422, 1955.

Patients suffering from diabetes mellitus may be cured or show dramatic improvement in sugar tolerance after living on a low-fat diet.

Eighty patients (74 of them males) with insulin-sensitive diabetes were treated in this series on optimal caloric diets containing 20–30 g of fat daily, 120–150 g of protein, and the rest carbohydrate; grossly underweight patients received as much as 4000 to 4500 calories daily; in the remainder, energy intake varied from 1000 to 2200 calories. Insulin was progressively reduced.

Fifty of the patients became "sugar-free" in from three to six weeks and eight more in 18 weeks. These 58 subjects required no further insulin. Six more required 10 units daily and six severe diabetics had their insulin requirements reduced from 80–120 units to 20–40 units.

Ten patients who had become "sugar-free" on diet alone showed increased carbohydrate tolerance, and one patient, a woman, who had initially required 20 units of insulin a day, became hypoglycemic after four years of treatment by a low-fat diet alone. The dietary regime and results are presented in detail.—F. E. HYTTEN

The attractive but controversial method of free diet treatment of diabetes in children continues to hold a number of adherents. For those who maintain that careful regulation of diabetes is necessary to promote longer and healthier lives for their patients, this method has no appeal. It appears that there is no immediate solution to this troublesome problem.

A Study of the Late Complications of Juvenile Diabetes in Approximately One Hundred Cases Using a "Free" Diet. W. W. Payne. *A.M.A. Am. J. Dis. Child.* 90: 550, 1955. (Soc. Trans.)

The late complications of juvenile diabetics who were on a "strict" diet from 1926 to 1936 are compared with those on a "free" diet since 1936.

On the free diet the child may eat as much as he likes of the simple foods used by his family, but meal times should always be regular and the intake of table sugar, jam, sweet cakes, and chocolate should be restricted. With regard to diabetic control, a complete absence of all symptoms and normal growth were considered essential. As far as possible, one dose of insulin a day was employed in a combination to obtain maximum freedom from glycosuria without hypoglycemic symptoms. Objectives were absence of significant ketonuria and blood sugar levels of less than 25 mg per 100 ml three hours after a meal.

The cases were divided into three groups according to the degree of control achieved. They were examined for eye, kidney, vascular, and neurologic involvement. In common with others the author found a well-marked correlation between the duration of diabetes and retinitis and a slight correlation between control and retinitis. There were very few cases of renal involvement or hypertension, and none showed neurologic or peripheral vascular changes clinically.

The majority of parents and children cooperated well when this liberal diet was used, and the control obtained by the "free" diet was as good and often better than that with a restricted diet in those patients who were changed over from weighed diets in the late 1930's.

Comparison with reports of the outcome in similar groups of children treated by stricter methods of dieting in other clinics shows the overall results to be no worse on the "free" diet, and probably somewhat better.

This controversial problem was discussed by Dr. George M. Guest, who was in agreement with the author. Dr. Hubble of England felt that the diet was somewhat irrelevant and that the more important problem involves assuring that adequate insulin is present in the metabolic pool throughout 24 hours. Dr. Richard Wagner of Boston pointed out that complications of equal severity may be observed among groups with excellent dietary control, as well as among "habitual diet breakers." He feels, in view of inadequate knowledge concerning the development of complications, that reasonable diets with not too rigid restrictions should be adhered to. Dr. Robert L. Jackson, an advocate of controlled and adequate diet, has extended his observations of 1948 and stated that there continues to be a high correlation between the incidence and severity of the degenerative changes and the degree of control of the disease.—J. N. ETTELDORF